AUG 28 1933

Madison Is the Convention City from August 21st–September 2nd. Plant Science Seminar, August 21st–25th. National Conference of Pharmaceutical Research, August 26th. American Association of Colleges of Pharmacy and National Association of Boards of Pharmacy, August 28th and 29th. Other Divisions from August 29th–September 2nd.

Vol. XXII, No. 8 AUGUST, 1933

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

TRADE MARK

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THE 81st ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN MADISON, WISCONSIN, AUGUST 28 TO SEPTEMBER 2, 1933, HOTEL LORAINE, HEADQUARTERS, EMERSON STANLEY, 602 CENTRAL BUILDING, MADISON, LOCAL SECRETARY.

The 1933 Meetings of the American Association of Colleges of Pharmacy, the National Association of Boards of Pharmacy, Conference of Pharmaceutical Association Secretaries, of the Pharmaceutical Law Enforcement Officials and the Plant Science Seminar will also be held in Madison.

Entered as second-class Matter, January 23, 1917, at the Post Office at Easton, Pa., under the Act of March 3, 1879. Acceptance for mailing at special rate of postage provided for in section 1103. Act of October 3, 1917; authorized July 10, 1918.

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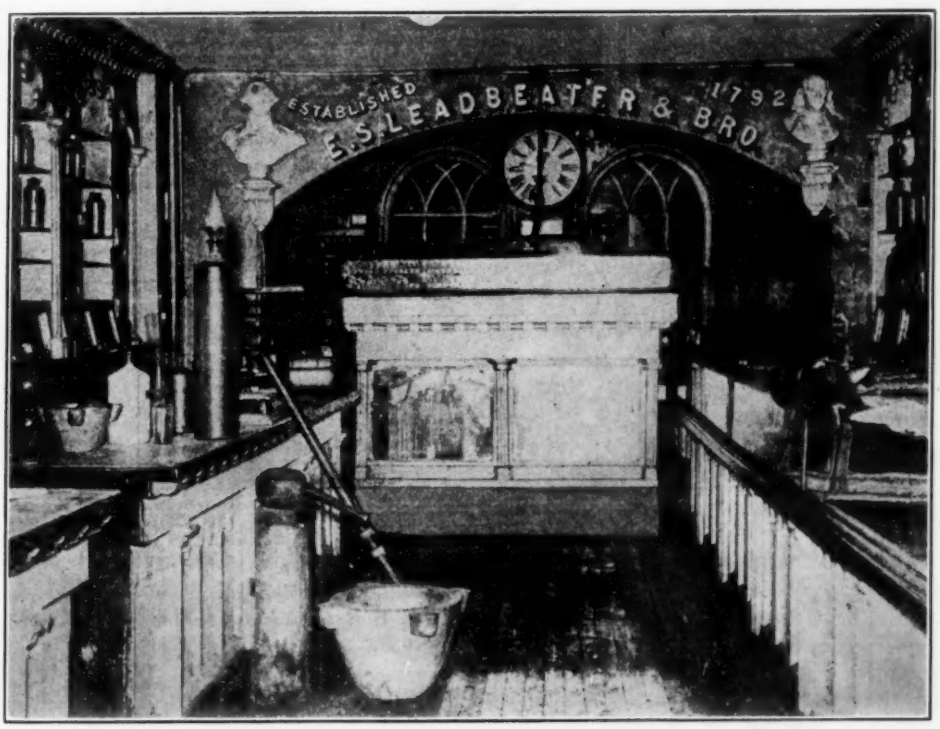
CHEMICAL WORKS

ST. LOUIS • MONTREAL • NEW YORK

Auction Sale of Leadbeater Pharmacy, Alexandria, Va., July 19, 1933. The sale took place in a room next to the old pharmacy.



Leadbeater Pharmacy, Alexandria, Va., before sale. The famed spirit of nitre bottle is on the counter, also a show bottle. On the front counter, at the left, is the General Robert E. Lee plate.

EDWARD STABLER.

Founder of Edward Stabler, successors are: E. Stabler & Son, William Stabler, William Stabler & Co., W. Stabler & Bro., John Leadbeater, J. Leadbeater and Son, Leadbeater & Co., E. S. Leadbeater & Co., E. S. Leadbeater & Bro., E. S. Leadbeater & Sons, Leadbeater Drug Corporation—1792–1933.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XXII AUGUST, 1933 No. 8

EDWARD STABLER.*

THE stock which laid the foundation of Edward Stabler's pharmacy in Alexandria was invoiced at 96£ 2s. and 3d. It was bought through the agency of Townsend Speakman, wholesale druggist of Philadelphia, June 25, 1792. The latter cautioned the buyer to reduce quantities ordered, "apprehending it most for thy interest for thee to have smaller quantities at first...till thou hast had some experience." The venture was a success—the stock, purchased by note, was paid for and doubled by the end of the first year, and the young apothecary married Mary Pleasants.

The first stock included three-quart flint-glass bottles with glass stoppers, at 5 shillings each. Two of these bottles disappeared—one remains, which was billed as containing spirit of nitre and is part of the purchase for the AMERICAN PHARMACEUTICAL ASSOCIATION. An association in Alexandria contemplates establishing a museum in the store room and keeping it open for the public; if so, it is tentatively agreed that the articles purchased will remain in Alexandria so long as the museum is maintained. If not, the items will be moved to the Headquarters Building in Washington.

The clock dates back to the earlier years of the pharmacy. There are many records, books, orders, prescriptions, etc., which connect the history of the pharmacy with the present. A plate on the front counter records where Robert E. Lee received orders to proceed to Harpers Ferry to apprehend John Brown.

* Edward Stabler's earlier pharmaceutical experience was gained in the drug store of his brother, William, at Leesburg, Va. The first of the Leadbeaters came to Alexandria in 1830 and engaged with William Stabler, son of Edward, who had succeeded to the business. In 1835, John Leadbeater married a daughter of Edward Stabler and became a partner in the firm of William Stabler and Bro. in 1844, and sole owner in 1852.

EDITORIAL

E. G. EBERLE, EDITOR 10 West Chase Street, BALTIMORE, MD.

THE PHŒNIX AS AN NRA EMBLEM.

THE NRA emblem has been interpreted as being that of a phœnix or of an eagle, more commonly designated as the "Blue Eagle." Seemingly it represents a phœnix and this mythical bird, adopted by the alchemists as their emblem, was during later periods a sign frequently used by pharmacists. "Wooton's Chronicles of Pharmacy" states that "according to Herodotus the Egyptians worshipped this bird; it was about the size of an eagle, with purple and gold plumage and a purple crest, its eyes sparkled like stars." Arising from its ashes the phœnix was perpetuated, thus it is an insignia of purification which may be acceptable as an emblem of pharmacy.

The President may have had the thought in mind as a symbol of resurrection from the ashes of past follies, which is essential to the restoration of national prosperity. The follies of the past years have been responsible, to a large extent, for the conditions which disturb us and recovery must come about by correction of methods which seek unfair advantages prompted by selfishness and greed and, to some extent, undermined confidence in activities, the success of which is largely dependent on public confidence. No doubt individuals and groups knew that eventually the penalty for selfish acts would have to be paid, but they were hopeful that somehow or other payment would be long deferred and, in the meantime, there would be gradual improvement; but to an extent conditions were so disturbing that "surgery" or "rejuvenation" as ascribed to the phœnix were deemed necessary. It will require not only all the skill, strength and patriotism of the officials in charge, but of those engaged in the industries and of all citizens to make the recovery plan effective. Codes are essential, but also a determination to establish better conditions and uphold them, and to that end the public must take a greater interest in forcing compliance with honest practices. The public has been largely responsible for the conditions because of indifference, selfishness and greed. "This 'bird of promise' will benefit those who adopt the insignia in good faith. It will benefit most those who, looking, striving upward, leave farthest behind the taint of practices deservedly left in the past." As we view it, the quoted lines express thoughts, far-reaching in their meaning and interpretation.

INTERPRETING THE CODES.

AS previously stated, President Roosevelt exempted from "maximum hours" requirement *registered pharmacists* and other professional persons employed in their profession and those employed in a management or executive capacity for more than $35.00 per week. In all probability, those who are engaged in pharmaceutical service other than as above will be included, but persons employed in the drug stores for work which does not link them with pharmaceutical engagements will have to be provided for under codes that limit the hours of work. It

is not intended to discuss this phase of the situation because codes have been under consideration and some temporarily in effect. While all divisions of the drug industry are closely related to pharmacy the exemption provided for pharmacists is very important and relieves pharmacists of an embarrassing situation, which would have meant a heavy burden; this has been a matter of great concern and received the attention of the AMERICAN PHARMACEUTICAL ASSOCIATION.

Naturally, disagreements have arisen on other questions which will not be commented on; the Department seems to be devoting its efforts to enforcement of the principle that no special interest shall make use of the National Industrial Recovery Act to gain an advantage over another. In discussing the subject of "Definite Business Improvement" the *Oil, Paint and Drug Reporter* says: "The Administration's move for economic improvement purposes one other achievement (in addition to the creation of a favorable mental attitude). It seeks to remove from business life the influences that have prevented the permanency of prosperity, or, at least, the maintenance of a higher average level of the common welfare. It is this purpose alone that differentiates the recovery now in progress from that which marked the passing of previous depressions. It is this purpose that seeks recovery that will stay; that will be mentally proof against the idea that slumps must come and then must run their supernaturally appointed course. Business must see this greater purpose in the planning of economic progress. It must lend its aid to the attainment of the purpose, seeking continued good rather than immediate benefits, better, yes, but fleeting."

A result for the good of the public should come out of this adjustment in restricting the sale and dispensing of medicines to those qualified by education and training. Times like the present bring to the fore a realization of conditions which have not heretofore been disturbing factors and it is to be hoped that the public will gain a clearer appreciation of the fundamentally important rôle of pharmacy for its protection.

THE MADISON MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

THE programs of various sections are being completed and promise a most interesting meeting. Consult the June and July JOURNALS, and the number for August presents many additional papers. Aside from the sections the Conferences of Pharmaceutical Law Enforcement Officials and of the Pharmaceutical Association Secretaries promise discussions of interest to every pharmacist. The programs heretofore printed will acquaint the readers with topics that are subjects for important discussions. The following titles are part of the program of Law Enforcement Officials and bespeak the interest of all who will attend the Madison meeting; all of them will be introduced by contributors well and favorably known to pharmacists. In the list are:

"A Legislative Attempt to Restrict the Opening of New Drug Stores," "The Value of Annual Renewal of Pharmacists' Certificates Is the Enforcement of Pharmacy Laws," "A Legislative Attempt to Establish Prescription Tolerance," "What Privileges Should Be Granted Unregistered Dealers under the Pharmacy

Law?" "The Need for Strict Enforcement of the Law," "Restricting the Practice of Pharmacy to Proper Persons," "The Importance of Synonyms in the Enforcement of Drug Standards and Their Relationship to the Enforcement of Pharmacy Laws," "The Proposed Amendments to the National Food and Drugs Act," "Narcotic Legislation in 1932–1933," "The Proper Enforcement of Fair Practice Codes for the Drug Industry under the National Industrial Recovery Act, General Enforcement Procedure and Technic."

Those who attend will have the opportunity of visiting the Chicago World's Fair. Attractive rates have been made to Chicago and return, and tickets on the Certificate Plan from Chicago to Madison and return may be purchased, permitting a stop-over.

"Wisconsin can probably lay claim to more varieties of scenery than any other state in the Union. Here are the gentle, rolling prairie lands; the rounded hills of the Kettle Moraine country in southeastern Wisconsin; the great lakes regions of the north which are sprinkled with lakes like the stars in the heavens, and criss-crossed with streams which vary from lazily flowing rivers to rushing torrents and cataracts like the Flambeau, the Brule, the Chippewa and others; Bayfield and the Apostle Islands in Lake Superior; the wind-carved hills of the dune country; Lake Winnebago, the largest inland lake entirely within the borders of a single state; the unglaciated area of the southwest, also called the driftless area; the bluffs of the Mississippi, one of the rarest sights in the world, and compared by travelers with the Rhine and the Hudson; the Dells of the Wisconsin, and the Dalles of the St. Croix. It would have been well-nigh impossible to have crowded within the limits of 56,000 square miles more beauty and more varieties of magnificent scenery than rightfully belongs to Wisconsin."

Madison is a beautiful university city, located among four lakes, and the Local Committee has arranged many entertainments for the visitors. Make your arrangements for the meeting without further delay—you will have the benefits of the convention and an enjoyable outing and, in addition, the opportunity of seeing the great World's Fair.

MADISON HOTEL RATES FOR A. PH. A. CONVENTION.

Loraine (Headquarters), with bath, single, $2.50–$4.00; double, $4.50–$7.00. Without bath, single, $2.00–$3.50.

Park Hotel, with bath, single, $2.50–$3.00; double, $4.00–$6.00. Without bath, single, $1.50–$2.00; double, $3.00–$3.50.

Belmont, with bath, $2.50–$5.50. Without bath, $2.00–$3.50.

Madison, with bath, $2.00–$2.50. Without bath, $1.00–$2.00.

Capitol, with bath, $1.50–$2.50. Without bath, $1.00–$2.00.

Cardinal, with bath, $1.75. Without bath, $1.00–$1.25.

Fess Hotel, $1.25–$2.00.

The Sherman Hotel at Randolph and Clark has been selected as Chicago headquarters for members stopping over in Chicago. The following rates are quoted by the Sherman Hotel: Single, $3.00; double, $5.00; double, twin beds, $6.00.

SCIENTIFIC SECTION

BOARD OF REVIEW ON PAPERS.—*Chairman*, L. W. Rowe; John C. Krantz, Jr.; F. J. Bacon.

THE RELATION OF SOME PHYSICAL PROPERTIES TO BACTERICIDAL ACTION OF SOME α-PHENYLSUBSTITUTED ACIDS.

BY L. H. BALDINGER AND J. A. NIEUWLAND.

Duggan (1) has shown that in the fatty acid series with increasing length of side chain there is a decrease in the antiseptic action. Using *Bacillus subtilis* as the test organism, he found that seven per cent formic acid, nine per cent acetic acid and twelve per cent propionic acid were required to restrain the growth of the organism. Siegler and Popenoe (2), (3) while investigating the action of fatty acids on green apple aphid found that the toxicity of the aliphatic acids increased with the molecular weight, reaching a practical toxicity at the C_6 acid. Tattersfield (4), using a different organism, later reported an increasing toxicity in the fatty acid series up to undecylic acid. According to his work, some correlation was shown between certain physical properties and toxicity. Loeb (5), while investigating the action of acids on the eggs of the sea urchin, found that the permeability of the cell membrane varied with the chemical constitution of the acid, thereby accounting for the varying toxicity. He also reported that the undissociated molecule of the acid appeared to constitute the toxic agent against the organism used. Similar relationships as to the disinfectant action of undissociated molecules have been shown by Ishiwara (6), Halvorson and Cade (7) and Levine, Peterson and Buchanan (8).

Laws (9), using a series of phenylsubstituted acids, observed that the converse of Duggan's results held for this type of acid. He found that phenylacetic acid showed a bactericidal action more than twice as strong as phenol, β-phenylpropionic acid three times that of phenol and γ-phenylbutyric acid five times that of phenol. Daniels and Lyons (10) prepared a series of ω-phenylsubstituted acids and determined certain physical constants of solutions of these acids, correlating these constants with the relative bactericidal action of the acids using *B. coli* and *B. typhosus* as test organisms. They found that the type of curve presented by the solubilities, the distribution coefficients, adsorption on activated charcoal, quite closely paralleled the curve presented by the bactericidal action. They found the surface tension lowered constantly with increase in molecular weight.

Having available a fairly convenient method for the preparation of a series of α-phenylsubstituted acids, it was decided to determine the relative bactericidal power of each of the acids and to compare this with some physical properties of their solutions, namely, solubility, adsorption on animal charcoal, distribution coefficient between oil and water and surface tension. While benzoic acid cannot, strictly speaking, be considered a member of this series, it was included in the tests. In the preparation of the graphs throughout this work the following abbreviations have been used:

B = Benzoic acid
A = Phenylacetic acid
P = α-Phenylpropionic acid
Bu = α-Phenylbutyric acid
V = α-Phenylvaleric acid
C = α-Phenylcaproic acid
H = α-Phenylheptoic acid

EXPERIMENTAL.

Preparation of the Acids.—The nitriles of the acids, with the exception of benzoic and phenylacetic, were prepared by the sodium-liquid ammonia method (11). The nitriles were then hydrolyzed by a slightly modified procedure of Pickard and Yates (12), which gave much better results than the alkali hydrolysis as recommended by Bodroux and Taboury (13). The procedure was as follows:

The nitrile was refluxed for eight or nine hours with moderately strong sulphuric acid (3:2). In order to prevent violent bumping of the mixture a glass tube, drawn into a capillary, was inserted through the stopper of the reaction flask so that the capillary dipped into the lower acid layer. A fine stream of dry air was passed through the mixture during the refluxing. The mixture was diluted with water and extracted with ether. The organic acid was then removed from the ether by extraction with ten per cent potassium hydroxide solution. This alkaline solution was then acidified with dilute sulphuric acid and extracted with ether to remove the organic acid. After drying the combined ethereal extracts over calcium chloride, the ether was distilled over a water-bath, and the acid distilled under reduced pressure.

All of the freshly distilled acids were clear, viscous liquids with a manure-like odor. The α-phenylbutyric, valeric and heptoic acids, upon cooling and standing, solidified to masses of crystals. The first two members of the series to be examined, benzoic acid, m. p. 121.5–122° C. (corr.) and phenylacetic acid, m. p. 77.2–77.7° C. (corr.), were Eastman Kodak products, recrystallized from hot water. When cooled in liquid ammonia, the liquid members of the series solidified but did not crystallize. The α-phenyl derivatives of propionic, butyric and valeric acids have been prepared by previous workers by the hydrolysis of the corresponding nitriles. The boiling points and analyses of the acids prepared in our work are given in Table I.

TABLE I.

α-Phenyl- Derivative of.	B. P. (corr.).	Formula.	Carbon, %. Calc.	Carbon, %. Found.	Hydrogen, %. Calc.	Hydrogen, %. Found.
n-Propionic acid	$132–34_8$	$C_9H_{10}O_2$	71.9	72.4	6.67	6.59
n-Butyric acid	$141–44_8$	$C_{10}H_{12}O_2$	73.2	73.1	7.32	7.34
n-Valeric acid	$153–57_7$	$C_{11}H_{14}O_2$	74.2	73.8	7.86	7.66
n-Caproic acid	$161–65_7$	$C_{12}H_{16}O_2$	74.8	74.7	8.32	8.25
n-Heptoic acid	$179–82_{11.5}$	$C_{13}H_{18}O_2$	75.7	76.0	8.73	8.55

Solubilities of the Acids.—The solubilities of the acids were determined at 30° C. and 40° C., using a rotating apparatus, similar to that described by Noyes (14), carrying four sixty-cubic centimeter wide-mouth bottles. The entire apparatus was immersed in a thermostat, capable of temperature control to within five-hundredths degree. Fifty cubic centimeters of boiled distilled water were placed in each bottle together with an excess of acid, the solubility of which was to be determined. The bottles were rotated from five to six hours at the desired temperature and then placed in an upright position in the bath to permit clarification. A pipette, to which was attached a cotton-filled bulb for filtration, was used to remove portions of the solution from each bottle. These portions were run into dry, tared, glass-stoppered weighing bottles and weighed. The contents of each bottle were titrated with $N/100$ sodium hydroxide, using phenolphthalein as an indicator. Before titration dry oxygen was bubbled through the solution to displace carbon dioxide. See Table II and Fig. 1.

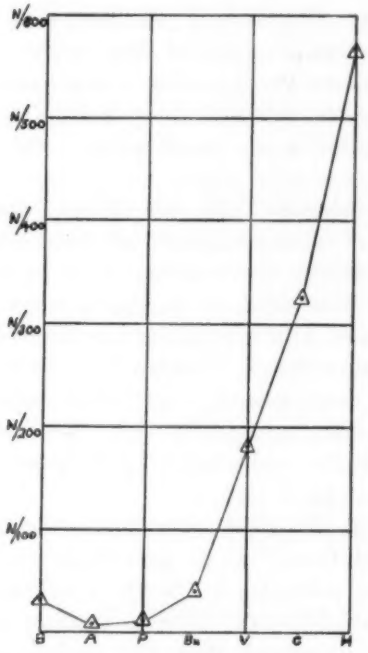


Fig. 1.—Solubilities of acids expressed as molalities at 30° C.

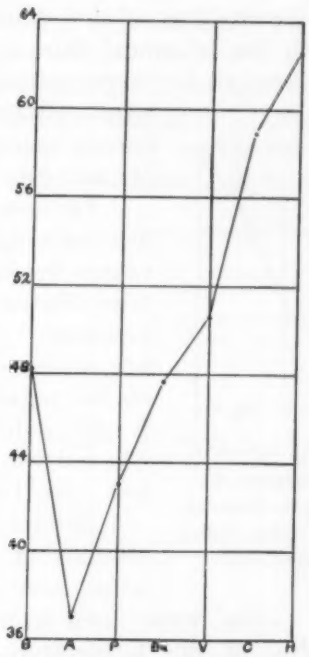


Fig. 2.—Distribution coefficients, C_2/C_1, of acids between animal charcoal and water, using $N/600$ solutions.

TABLE II.—SOLUBILITIES OF ACIDS EXPRESSED IN GRAMS OF ACID DISSOLVED IN ONE HUNDRED GRAMS OF WATER.

Acid.	30° C.	40° C.
Benzoic	0.408	0.552
Phenylacetic	2.068	3.334
α-Phenylpropionic	1.2154	1.3325
α-Phenylbutyric	0.4230	0.4445
α-Phenylvaleric	0.0978	0.1854
α-Phenylcaproic	0.0591	0.0633
α-Phenylheptoic	0.0365	0.0416

Adsorption of Acids on Bone Black.—The adsorption of the acids on animal charcoal was determined using $N/100$ solutions of the acids as starting concentration wherever possible and approximately saturated solutions in other cases. The high dilutions of acids used rendered duplication of values very difficult, but by determining the coefficients of all the acids at one time under approximately constant conditions, values were obtained from which could be plotted a curve showing the variation in adsorption with increase in molecular weight. It will be observed that the ratio of the concentrations, *i. e.*, C_2/C_1, is not a constant but increases with decrease in concentration. From the data obtained, it appears that the adsorption process follows an equation similar to that of Freundlich (15), $ln C_2 = ln k + \frac{1}{n} ln C_1$. Widely varying values for the constants k and n were obtained when the data observed was substituted in the adsorption formula.

To twenty-five cubic centimeters of the diluted acid solutions was added one-tenth Gm. of animal charcoal and the solutions agitated thoroughly at five-minute intervals for twenty minutes, filtered, and twenty cubic centimeters of the filtrate titrated with $N/100$ sodium hydroxide from a microburette using phenolphthalein as an indicator. See Table III and Fig. 2.

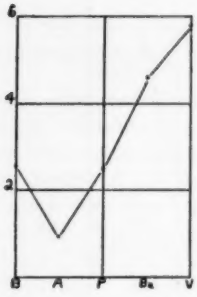


Fig. 3.—Distribution coefficients, C_2/C_1, of acids between oil and water, using $N/600$ solutions.

Partition Coefficient between Oil and Water.—Twenty-five cubic centimeters of fresh cottonseed oil were added to twenty-five cubic centimeters of a solution of the acid. The same dilutions of acids were used as in the adsorption experiments. The oil and solution mixture was rotated for five hours at room temperature. Twenty cubic centimeters of the aqueous layer were pipetted off and titrated with $N/100$ sodium hydroxide, phenolphthalein as indicator. The last two members of the series were not included in this test. See Table IV and Fig. 3.

Surface Tension of the Acid Solutions.—The surface tensions of $N/600$ solutions, so as to include the entire series, were determined using a du Nouy Tensiometer at 24.5° C. The water used in making the dilutions gave a reading of 73.7 dynes/cm. at this temperature. It was observed that the surface tension

TABLE III.—ADSORPTION ON ANIMAL CHARCOAL EXPRESSED BY THE VALUES OF C_2/C_1.

C_2 = Millimols of solute per Gm. of animal charcoal.
C_1 = Millimols of solute per milliliter of solution.

Normality.	B.	A.	P.	Bu.	V.	C.	H
1/100	8.81	7.8	9.44	10.8	..	..	..
1/200	20.05	14	19.65	18.9	..	..	..
1/300	30.85	19.7	22.7	25.2	26.3	..	..
1/400	38.4	31	27.5	30.5	35.5	24.5	..
1/500	46.7	36.8	41	34.1	41.6	39.6	..
1/600	48.2	37.1	43.1	47.7	49.6	58.8	62.5

TABLE IV.—PARTITION COEFFICIENT C_2/C_1 BETWEEN OIL AND WATER.

C_2 = Gm. acid per twenty-five cubic centimeters of oil.
C_1 = Gm. acid per twenty-five cubic centimeters of solution.

Normality.	B.	A.	P.	Bu.	V.
1/100	5.55	1.93	4.31	11.14	..
1/200	4.96	1.58	3.9	8.48	..
1/300	3.85	1.55	3.25	5.98	7.12
1/400	3.09	1.24	2.98	5.08	6.61
1/500	3.03	1.15	2.64	4.78	5.96
1/600	2.64	0.96	2.54	4.63	5.77

of the water was lowered by all of the acids but no definite relationship between increasing side chain length and surface tension lowering could be inferred from the data obtained. It is a well-known and recognized fact that surface tension lowering does not alone serve as a criterion for a good antiseptic, but that other factors may enter into the bactericidal action.

Bactericidal Values of the Acids.—Proper dilutions of the acids were made from relatively concentrated solutions. Phenylheptoic acid could not be included

in the tests because of limiting solubility. The test organism used was a 22–26-hour culture of *Bacillus coli* (*Harris strain*), incubated and grown at 37.5° C. on nutrient broth. The stock culture was carried on agar slants of the same composition as the broth medium plus one and one-half per cent agar. When the test organism had not been transferred daily, four or five daily transfers were made before using it for testing purposes. Transfers and inoculations were made with a four-millimeter loop. Five-tenths cubic centimeter of a suspension of *B. coli* was added to four and one-half cubic centimeters of nutrient broth. One-tenth cubic centimeter of this suspension was then added to five cubic centimeters of the acid solutions. The organism was allowed to stand in the acid solution for an hour at 37.5° C. and was then inoculated into nutrient broth and incubated for forty-eight hours at 37.5° C. A test with phenol was added as a comparator for bactericidal action. See Table V and Fig. 4.

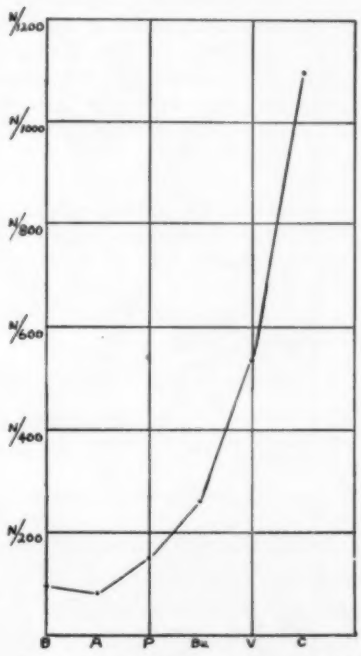


Fig. 4.—Bactericidal values of acids expressed as normalities.

DISCUSSION.

It will be observed that an unlimited increase in germicidal activity with increasing molecular weight is prevented by the decreasing solubility which also accompanies increasing molecular weight. With this series and the test organism used, the practical bactericidal efficiency appears to reach a maximum at the C_6 acid. All of the series, with the exception of benzoic acid, are expensive or difficult to prepare, and have a disgusting odor, two factors which would limit their use as practical antiseptics.

As pointed out by Tattersfield (4) and Daniels and Lyons (10), no one of the physical properties entirely accounts for the toxicity shown by the fatty acids.

TABLE V.—DILUTIONS OF ACIDS WHICH WILL INHIBIT THE GROWTH OF *B. coli* IN ONE HOUR.

Acid.	Dilution.	Acid.	Dilution.
Phenol	1–180	α-Phenylbutyric	1–1600
Benzoic	1–800	α-Phenylvaleric	1–3000
Phenylacetic	1–600	α-Phenylcaproic	1–5700
α-Phenylpropionic	1–1000		

SUMMARY.

1. By the hydrolysis of the corresponding nitriles, a series of α-phenyl-substituted acids has been prepared, and their solubilities determined in water at 30° C. and 40° C.

2. The curves showing the solubilities of the acids, the adsorption by animal charcoal of the acids from their aqueous solutions and the distribution coefficients between oil and water parallel that of the bactericidal action of the series, using *B. coli* as the test organism.

3. The bactericidal action of these acids appears to be a function of solubility, side chain length, adsorption by animal charcoal distribution coefficient between oil and water and surface tension lowering.

LITERATURE CITED.

(1) Duggan, *Amer. Chem. J.*, 7 (1885–1886), 62.
(2) Siegler and Popenoe, *J. Agr. Research*, 29 (1924), 259.
(3) Siegler and Popenoe, *J. Econ. Entomol.*, 18 (1925), 292.
(4) Tattersfield, *J. Agri. Sci.*, 17 (1927), 181; *Ann. Appl. Biol.*, 14 (1927), 231.
(5) Loeb, *Biochem. Z.*, 15 (1909), 254-271.
(6) Ishiwara, *Z. Immunitäts.*, 40 (1924), 429.
(7) Halvorson and Cade, *Proc. Soc. Exptl. Biol. Med.*, 25 (1928), 506.
(8) Levine, Peterson and Buchanan, *Ind. Eng. Chem.*, 20 (1928), 63.
(9) Laws, *J. Physiol.*, 17 (1894–1895), 360; *Chem. News*, 71 (1895), 15.
(10) Daniels and Lyons, *J. Phys. Chem.*, 35 (1931), 2049.
(11) To be published in the *J. Am. Chem. Soc.*, July issue, 1933 or later.
(12) Pickard and Yates, *J. Chem. Soc.*, 95 (1909), 1017.
(13) Bodroux and Taboury, *Bull. soc. chim.*, 7 (1910), 666, 670, 732.
(14) Noyes, *Z. physik. Chem.*, 9 (1892), 606.
(15) Freundlich, *Ibid.*, 57 (1907) 385.

DEPARTMENT OF CHEMISTRY,
NOTRE DAME, INDIANA.

THE CONSTITUENTS OF WU CHÜ YÜ (*EVODIA RUTÆCARPA*).*

BY A. LING CHEN AND K. K. CHEN.

Wu Chü Yü is the fruit of a shrub and has been used for a long time in Chinese medicine as a drug for the treatment of headache, abdominal pain, dysentery, cholera, worm infestations and postpartum disturbances (1). Botanically, the plant has been identified as *Evodia rutæcarpa*, family rutaceæ (2). The crude drug is easily available from Chinese drug stores. Our supply came from Tientsin, China. Each fruit consists of small black carpels, five in number, with short stalks, weighs on the average 10.3 mg., has an aromatic odor and is hot and bitter to the taste, similar to black pepper.

Chemical studies on Wu Chü Yü have been undertaken by several Japanese investigators. Keimatsu (3) reported the isolation of an indifferent crystalline substance, having the empirical formula $C_{18}H_{22}O_6$, which he named evodin. Asahina and Ishio (4) presented evidence that the formula of evodin was $C_{17}H_{20}O_9$. In addition, Asahina and Kashiwaki (5) succeeded in isolating two alkaloids, evodiamine and rutæcarpine, having the formulas $C_{19}H_{17}ON_3$ and $C_{18}H_{13}ON_3$, respectively. During the following fourteen years, Asahina and his associates published data on the chemical structures of both evodiamine and rutæcarpine, and finally their syntheses (6), (7), (8), (9), (10), (11), (12), (13).

Our chief interest in Wu Chü Yü was to obtain in an amount sufficient for pharmacological study the principles known to be present in the fruit. In the process of separation, we obtained evodiamine and rutæcarpine, and by elementary analyses and molecular weight determinations we confirmed Asahina's formulas. With regard to the non-nitrogenous substance, evodin, our results differ from those

* From the Lilly Research Laboratories, Eli Lilly and Company, Indianapolis.

of Keimatsu (3) and Asahina and Ishio (4). Furthermore, we isolated a fourth compound which contains nitrogen and has the provisional formula, $C_{13}H_{13}O_2N$. We named it wuchuyine.

Our pharmacological work has been deferred because of the fact that the four substances are very slightly soluble in water and do not easily form soluble salts or derivatives, and it therefore appears desirable to make a brief report of our chemical findings at the present time.

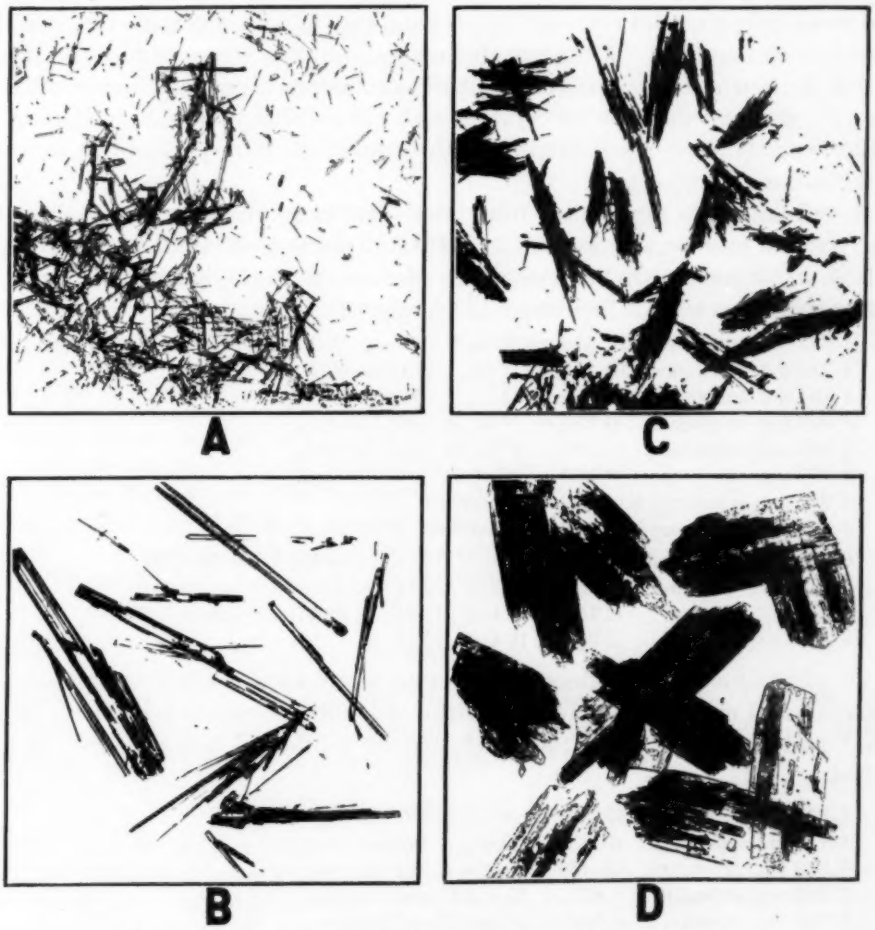


Fig. 1.—Crystalline forms of the constituents of Wu Chü Yü.

A. Rutæcarpine
B. Evodiamine
C. Wuchuyine
D. Evodin

EXPERIMENTAL.

Five Kg. of the pulverized material were percolated with acetone until extraction was almost complete. The acetone of the percolate was removed by distillation under diminished pressure, and the syrupy liquid was treated with a 2.5 per cent solution of sodium hydroxide and a small volume of ether, both of which dissolved out large amounts of impurities. A mass of yellow powder which con-

tained a mixture of the four different constituents was separated by filtration under suction. This mass was dried, washed with ethyl alcohol and again filtered. The powder was then dissolved in hot acetone. Upon standing in an ice chest over night, a large crop of crystals of various forms was obtained.

A portion of the crystals was soluble in warm benzene and crystallized out upon cooling. This was found to be chiefly rutæcarpine and was purified by repeated crystallization from ethyl alcohol.

The benzene-insoluble fraction was treated with cold acetone. At this point there was a part that did not readily go into solution, so it was separated and dissolved in warm acetone. After repeated crystallizations, it proved to be evodin.

The acetone-soluble portion was subjected to slow evaporation and crystallization. By washing the crop of crystals with chloroform, in which evodiamine is soluble,* wuchuyine was separated. Both compounds were purified by repeated crystallizations from acetone.

A. Rutæcarpine crystallizes from ethyl alcohol in fine needles (see Fig. 1[1]), slightly yellow in color, melts at 261.5–262° C. (corrected), is optically inactive and is soluble in acetone, warm benzene and to a less extent in ethyl alcohol. A solution of rutæcarpine has a green fluorescence. Analysis:[2]

4.902 mg. substance: 13.570 mg. CO_2, 2.020 mg. H_2O
4.784 mg. substance: 13.230 mg. CO_2, 1.910 mg. H_2O
4.764 mg. substance: 13.155 mg. CO_2, 1.990 mg. H_2O
2.998 mg. substance: 0.383 cc. N at 24° and 758 mm.
2.946 mg. substance: 0.380 cc. N at 24° and 758 mm.
2.770 mg. substance: 0.360 cc. N at 23° and 750 mm.
0.238 mg. substance in 4.420 mg. camphor: 6.9°Δ
0.290 mg. substance in 5.590 mg. camphor: 6.9°Δ

$C_{18}H_{13}ON_3$ calculated: C 75.27, H 4.56, N 14.64, molecular weight 287
Found: C 75.52, H 4.61, N 14.63, molecular weight 312
C 75.45, H 4.47, N 14.77, molecular weight 303
C 75.39, H 4.68, N 14.79.

B. Evodiamine crystallizes from acetone as colorless needles, begins to soften at 265° C. and melts at 272–273° C. (corrected), has an optical rotation of $[\alpha]_D^{28.5}$ +251° and is soluble in acetone and slightly soluble in benzene and alcohol. Analysis:

4.840 mg. substance: 13.360 mg. CO_2, 2.470 mg. H_2O
4.732 mg. substance: 13.060 mg. CO_2, 2.410 mg. H_2O
4.888 mg. substance: 13.480 mg. CO_2, 2.510 mg. H_2O
3.067 mg. substance: 0.371 cc. N at 24° and 758 mm.
3.035 mg. substance: 0.364 cc. N at 23° and 758 mm.
2.918 mg. substance: 0.355 cc. N at 22° and 750 mm.
0.213 mg. substance in 3.810 mg. camphor: 7.2°Δ
0.200 mg. substance in 4.860 mg. camphor: 5.3°Δ

$C_{19}H_{17}ON_3$ calculated: C 75.22, H 5.65, N 13.83, molecular weight 303
Found: C 75.31, H 5.71, N 13.86, molecular weight 310
C 75.30, H 5.70, N 13.79, molecular weight 310
C 75.24, H 5.75, N 13.89.

[1] The microphotographs of the crystals were made by Mr. C. R. Eckler, to whom we are greatly indebted.

[2] The analyses reported in this paper were made by Dr. Ing. A. Schoeller, Berlin-Schmargendorf, Germany.

C. Wuchuyine crystallizes from acetone in small, colorless tufts, melts at 237.5° C. (corrected), has an optical rotation of $[\alpha]_D^{29.5}$ −68°, and is soluble in acetone and slightly soluble in alcohol. Analysis:

5.000 mg. substance: 13.240 mg. CO_2, 2.590 mg. H_2O
5.092 mg. substance: 13.480 mg. CO_2, 2.600 mg. H_2O
4.869 mg. substance: 12.860 mg. CO_2, 2.460 mg. H_2O
3.136 mg. substance: 0.167 cc. N at 23.5° and 762 mm.
2.991 mg. substance: 0.157 cc. N at 22.5° and 762 mm.
3.006 mg. substance: 0.159 cc. N at 22.5° and 762 mm.
0.348 mg. substance in 5.950 mg. camphor: 8.0°Δ
0.301 mg. substance in 4.650 mg. camphor: 8.9°Δ

$C_{13}H_{13}O_2N$ calculated: C 72.56, H 6.09, N 6.52, molecular weight 215
Found: C 72.24, H 5.80, N 6.15, molecular weight 292
C 72.24, H 5.71, N 6.09, molecular weight 291
C 72.07, H 5.65, N 6.13.

The above formula is given with reservation, especially since the analytical results do not entirely check with the theoretical values.

D. Evodin crystallizes from acetone in colorless plates, melts at 290.5–291° C. (corrected), has an optical rotation of $[\alpha]_D^{29.5}$ −131.4° and is only moderately soluble in acetone. Analysis:

4.898 mg. substance: 11.890 mg. CO_2, 2.830 mg. H_2O
4.948 mg. substance: 11.970 mg. CO_2, 2.820 mg. H_2O
4.875 mg. substance: 11.805 mg. CO_2, 2.830 mg. H_2O
0.354 mg. substance in 6.120 mg. camphor: 5.0°Δ
0.273 mg. substance in 5.100 mg. camphor: 4.5°Δ

$C_{26}H_{30}O_8$ calculated: C 66.39, H 6.89, molecular weight 470
Found: C 66.21, H 6.47, molecular weight 462
C 66.03, H 6.38, molecular weight 477
C 66.07, H 6.50.

SUMMARY

By a chemical study of Wu Chü Yü, or the fruit of *Evodia rutæcarpa*, four crystalline substances have been obtained: (*a*) *rutæcarpine*, $C_{15}H_{13}ON_3$; (*b*) *evodiamine*, $C_{17}H_{17}ON_3$; (*c*) *wuchuyine*, $C_{13}H_{13}O_2N$; and (*d*) *evodin*, $C_{26}H_{30}O_8$.

BIBLIOGRAPHY.

(1) S. C. Li, Pentsao Kang Mu (1596), Chapter 32.
(2) Botanical Nomenclature, Commercial Press (1917), page 437.
(3) K. Keimatsu, *Yakugakuzasshi* (*J. Pharm. Soc. Japan*), No. 248 (1902), 979.
(4) Y. Asahina and M. Ishio, *Yakugakuzasshi*, No. 404 (1915), 1148.
(5) Y. Asahina and K. Kashiwaki, *Ibid.*, No. 405 (1915), 1273.
(6) Y. Asahina and A. Mayeda, *Ibid.*, No. 416 (1916), 871.
(7) Y. Asahina and A. Fujita, *Ibid.*, No. 476 (1921), 863.
(8) Y. Asahina, *Ibid.*, No. 503 (1924), 1.
(9) Y. Asahina and T. Ohta, *Ibid.*, No. 530 (1926), 293.
(10) Y. Asahina and T. Ohta, *Ibid.*, 48 (1928), 313.
(11) Y. Asahina and T. Ohta, *Ibid.*, 49 (1929), 1162.
(12) Y. Asahina and T. Ohta, *Ber. deut. chem. Gesellsch.*, 61B (1928), 319.
(13) Y. Asahina and T. Ohta, *Ibid.*, 61B (1928), 869.

CHEMICAL STUDY OF TWO CHINESE DRUGS.*

BY DANIEL TSAO AND E. V. LYNN.

FANG FÊNG.

According to Stewart, "Chinese Materia Medica," fang fêng is obtained from *Siler divaricatum*, *Peucedanum rigidum* or *Peucedanum terebinthaceum*. It is found in most of the central and northern provinces. The stems are 2–3 feet high, the leaves are coriaceous and glabrous and the flowers are white and have five petals. Although all parts of the plant are used in medicine, the name chiefly refers to the root, which appears on the market in long, brownish yellow, irregularly branching pieces, often with some of the stem attached. It has a sweet, aromatic and mucilaginous taste.

The drug is given in all diseases due to damp and chill, in disorders of the circulation and in general debility, also to cure headache and dizziness attributed to chill. The name fang means "prevent" and fêng means "chill." It is also regarded as an efficient antidote in aconite poisoning.

The material employed in this investigation was bought in the open market. After being ground to a coarse powder, it was subjected to a proximate analysis by methods of the A. O. A. C. The results follow in per cent:

	I.	II.	Average.
Volatile at 100° C.	11.81	11.86	11.84
Total ash	4.33	4.40	4.34
Reducing sugars	6.48	6.31	6.40
Sucrose by reduction	3.23	3.15	3.19
Pentosans	11.51	11.42	11.46
Starch by acid hydrolysis	2.27	2.16	2.21
Starch by diastase	1.71	1.50	1.60

Two samples of 10 Gm. each were introduced into Soxhlet extractors and submitted to selective action with several solvents for 18 hours each. The residues left after spontaneous evaporation of the solvents were dried to constant weight in a desiccator, then the volatile portion in the first two was estimated by heating again to constant weight at 110° C. The results follow in percentage of dried material:

	I.	II.	Average.
Petroleum ether, total	2.23	2.13	2.18
volatile	0.51	0.51	0.51
Ether, total	1.16	1.32	1.24
volatile	0.36	0.41	0.38
Alcohol	7.93	7.87	7.90
Water	13.23	14.31	13.77

Tannin.—The alcohol was evaporated from a fluidextract made according to Type A, U. S. P. X, and the residue was taken up with water and filtered. Portions of the yellowish brown solution were tested with neutral ferric chloride solution, with potassium ferricyanide and ammonia water and with lime water. Since none of the reagents gave a positive reaction, one can presume that tannins are absent.

Alkaloid.—A fluidextract was made from 50 Gm. of the drug, using as solvent

* Scientific Section, A. PH. A., Toronto meeting, 1932.

an acidified mixture of alcohol and water (5:1). The filtered solution was made alkaline with ammonia and was extracted with ether-chloroform (2:1). The ethereal solution was then exhausted with normal sulphuric acid and this was treated with the following reagents: Scheibler's, Wagner's, Mayer's, Hager's, tannic acid T.S. and neutral tannin T.S. The first two gave slight precipitates which disappeared on standing, but the others gave none, indicating strongly that no alkaloid is present in the original drug.

Acids.—A mixture of 1 Gm. of the sample and 15 cc. of neutral alcohol was set aside for 24 hours and then filtered. The solution was titrated with tenth-normal sodium hydroxide using phenolphthalein as indicator. Calculated as acetic acid, the results were 1.77 and 1.85 per cent. An aqueous extraction in the same way gave 1.03 and 1.09 per cent. Tests of the distillate from the aqueous extraction showed that none of the acid is volatile. On the other hand, none of the water-soluble acid seemed to be withdrawn by ether. Silver sulphate gave only 0.13 per cent of precipitate, while silver nitrate was rapidly reduced in the cold to metallic silver. Attempts to precipitate the acid by calcium or barium were only partly successful, since the amount obtained was very small. The nature of the acid must remain for the time being undetermined.

Toxicity.—Several experiments were made on rats, using amounts of alcoholic and aqueous extracts equivalent to 1 Gm. of the drug per oral dose. In spite of this high amount, no abnormal symptoms could be observed during 12 hours after administration, and one is justified in assuming that the material is fairly safe.

Hsiung Ch'iung.

Much confusion in names seems to have occurred with this drug, since various parts of the plant and different varieties are given separate designations in Chinese materia medica. The root, which is the usual drug, is also called Ch'uan Hsiung, Hsiang Kuo and Hu Ch'iung. It is derived from *Conioselinum univittatum Turcz.* (*Cnidium officinale Makino*), an umbelliferous plant which is best cultivated. The active ingredient is a volatile oil which has been examined repeatedly and whose chief constituent seems to be a lactone. The roots are recommended for a great variety of ailments, such as colds, headaches, anemia, menorrhagia, retained placenta, sterility, pains and aches of all kinds, rheumatism, etc.

A sample of the roots bought in the open market was first subjected to proximate analysis, with the following results in percentage:

	I.	II.	Average.
Volatile at 100° C.	10.87	10.77	10.82
Total ash	3.05	2.98	3.01
Reducing sugars	None	..	..
Starch by acid hydrolysis	28.39	29.51	28.95
Protein (N × 6.25)	2.47	2.04	2.26
Ether extract	9.54	9.78	9.66
Crude fibre	4.80	4.57	4.68
Tannin	0.34	0.42	0.38

Qualitative tests for alkaloid, made as before, were negative. Results from selective extraction were as follows:

	I.	II.	Average.	
Petroleum ether, total	7.58	7.48	7.53	Yellow
volatile	0.75	0.55	0.65	
Ether, total	8.29	8.31	8.30	Yellow
volatile	1.16	1.28	1.22	
Alcohol	15.83	15.63	15.73	Brown
Water	16.43	16.43	16.43	Brown

The most interesting feature of the drug is the large amount of fixed oil which it contains. In order to examine this more closely an ether extraction was made of about 500 Gm. and the volatile oil was removed by distillation. The collected fat was then dried and its constants were determined. They are: specific gravity at 25° C., 0.94672; index of refraction at 25° C., 1.4821; acid number, 31.5 and 31.9 saponification number, 205.2 and 200.4; ester number, 171.1; unsaponifiable residue, 1.55 and 1.64; iodine number, 70.34 and 71.2; Reichert-Meissl number, 0.1; Polenski number, 0.25; solid acids, 10.78; liquid acids, 89.22; titer test, 24.3° C. Several drying experiments showed that the oil is only about 80 per cent as efficient as raw linseed oil.

The free fatty acids were isolated by saponification from 75 Gm. of the fat, giving about 70 Gm. of dried material, which had an index of refraction of 1.4781 at 25° C. This was submitted to distillation at 10-mm. pressure. The first portion, coming over at 50–60° C. was solid and gave a titer test of 56–57° C. From 60° to 117° only 0.5 Gm. distilled and then decomposition set in. The residue had an acetyl value of 11.42, indicating a high per cent of hydroxy acids.

Phytosterols.—During ether extraction there separated from the solution a white substance amounting to 0.6 per cent of the drug. From this ethyl acetate extracted an apparently pure substance melting at 182–183°, from the residue alcohol or chloroform withdrew one with a melting point of 207–207.5° and ether gave still a third material melting at 214.5°. Careful repurification did not seem to alter the melting temperatures, but mixtures of them gave much lower values. All of them gave reactions of the phytosterols but well-defined acetates could not be obtained; the white solids resulting gave indistinct melting points between 147° and 156° C. From the unsaponifiable residue there was obtained still a fourth phytosterol in the form of needles melting at 137° C. Lack of material prevented any further examination of these interesting materials.

SUMMARY.

Fang fêng contains no alkaloids or tannin and has no appreciable effect on rats even in high dosage. The chief constituents appear to be sugars, gums and free acids.

Hsiung Ch'iung contains chiefly fixed and volatile oils. The former is of the drying class and has a high content of hydroxy acids. From this drug were isolated several phytosterols.

SEATTLE, WASH.,
October 1, 1932.

The American Institute of Pharmacy is dedicated to those who have given of their thought and endeavor to the improvement of Public Health and to the further advancement of Science in Pharmacy.

THERAPEUTIC SUBSTANCES DERIVED FROM UNSYMMETRICAL DIPHENYL COMPOUNDS I.*

BY S. E. HARRIS AND W. G. CHRISTIANSEN.

SOME MERCURY DERIVATIVES OF 2- AND 4-HYDROXYDIPHENYL.

The studies of diphenyl compounds in this laboratory have included the preparation of a number of mercury derivatives of the following types, (*a*) from nitrated hydroxy-diphenyls, (*b*) from brominated hydroxy-diphenyl, (*c*) from diphenyl-phenolphthalein.

The compounds were tested for their activity against bacteria and were shown to have valuable bactericidal properties. Table I illustrates the activity against *B. Typhosus*, the second column giving the minimum concentration at which the organism is killed in five minutes. The mercury compound was dissolved in the smallest excess of NaOH which would give a clear solution at 1–500, and diluted with distilled water immediately prior to the test.

TABLE I.

Germicide.	Dilution Killing *B. Typhosus* in 5 Minutes.
2-Acetoxy-mercuri-3-nitro-4-hydroxy-diphenyl	1–2000
4-Acetoxy-mercuri-3,5-dinitro-2-hydroxy-diphenyl	1–1000
4-Anhydro-mercuri-5-acinitro-3-nitro-2-hydroxy-diphenyl	1–1000
4,6-Diacetoxy-mercuri-3,5-dinitro-2-hydroxy-diphenyl	1–2500
Diacetoxy-mercuri-4′-nitro-2-hydroxy-diphenyl	1–2500
Hydroxy-mercuri-3,3′-diphenyl-5,5′-dibromo-phenolphthalein	1–1250
Diacetoxy-mercuri-3,3′-diphenyl-5,5′-dinitro-phenolphthalein	1–2500
Monoacetoxy mercuri-3,3′-dinitro-phenolphthalein	1–1000
Diacetoxy-mercuri-3,3′-dinitro-phenolphthalein	1–500
2-Phenyl-4-bromo-6-acetoxy-mercuri-phenoxy-acetic acid	1–100

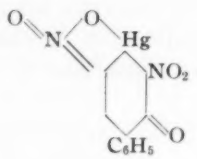
The mercury derivatives of nitrophenolphthalein were prepared for comparison with the corresponding derivatives of diphenyl-phenolphthalein, and it will be noted that the introduction of the phenyl groups considerably raises the germicidal activity. In addition to the compounds contained in the above table, the mercury derivatives of condensation products of 2-hydroxy-diphenyl with isatin were studied. These will be dealt with in a separate communication.

The preparation of the mercury derivatives offered few difficulties. Mercuration was carried out by treating a boiling alcoholic solution of the suitable intermediate with an aqueous solution of mercuric acetate acidified with acetic acid, and refluxing until a filtered test portion showed absence of ionic mercury when tested with aqueous NaOH or ammonium sulphide. The mercury derivatives were thus obtained as alcohol-insoluble powders which were purified by reprecipitation from filtered alkaline solutions by means of acetic acid. They were in all cases insoluble in the common organic solvents but some were slightly soluble in boiling glacial acetic acid. In no case was a melting point observed, complete decomposition without melting taking place at temperatures above 300° C. The solubility in aqueous alkalies showed wide variations, the mercury derivative of 5-bromo-2-hydroxy-diphenyl being completely insoluble even in a large excess of boiling NaOH.

* Scientific Section, A. PH. A., Toronto meeting, 1933.

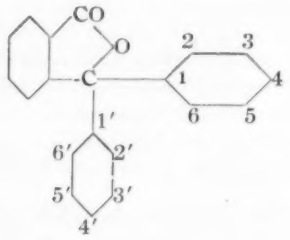
The mercury derivatives of the nitro-hydroxy-diphenyls and of the diphenyl-phenolphthaleins, however, were readily soluble in a moderate excess of alkali.

While the mercuration of 3,5-dinitro-2-hydroxy-diphenyl in alcohol solution proceeds normally, an attempt to mercurate this compound in aqueous acetic acid led to the formation of the anhydro-acinitro compound:



This dissolved in alkalies only on prolonged boiling. The structure was assigned on solubility in alkali, the analytical results and the strong orange color of the solid substance, both the mono- and dimercury derivatives of 3,5-dinitro-2-hydroxy-diphenyl being pale yellow.

No attempt has been made to establish the position taken by the mercury entering the molecule. In the simpler derivatives analogy with known cases has been assumed, while the diphenyl-phenolphthaleins offer a special problem. White (1) was unable to mercurate phthaleins in which 3,3′ and 5,5′ positions were all occupied



Under different experimental conditions, however, Greenbaum (2) prepared mercury derivatives of such compounds and assumed that the mercury entered the phthalic acid nucleus. We found that both 3,3′, 5,5′ tetra substituted and 3,3′ disubstituted phthaleins were mercurated with equal facility, although it was not always possible to introduce more than one mercury group, *e. g.*, into 3,3′-diphenyl-5,5′-dibromo-phenolphthalein. This would suggest that here the mercury enters the phthalic acid residue, while in the case of 3,3′-diphenyl-5,5′-dinitrophenol-phthalein, which readily yielded a dimercury derivative, one or both of the mercury groups enters a phenol nucleus.

Analysis for mercury was carried out by the method of Whitmore (3). The results were not entirely satisfactory and the method has been discarded in favor of a method described by Tabern and Shellberg in a private communication through the A. D. M. A. Committee on Synthetic organic chemicals.

Experimental.—2-acetoxy-mercuri-3-nitro-4-hydroxy-diphenyl. The preparation of this compound is typical of the general method and is described in detail.

21.5 Gm. of 3-nitro-4-hydroxy-diphenyl (4) were dissolved in 200 cc. of alcohol and the solution heated to boiling under reflux. 28.7 Gm. of mercuric acetate dissolved in 200 cc. of

water, acidified with 0.5 cc. glacial acetic acid were then slowly added to the boiling solution. Brisk agitation during the addition and subsequent boiling prevented the product from sticking to the sides of the flask. When a side test showed absence of ionic mercury the brick-red precipitate was filtered from the hot solution and washed with alcohol and ether. The yield was practically quantitative. On dissolving in boiling NaOH and cooling the sodium salt was thrown down as a scarlet powder, which was largely hydrolyzed when treated with water.

The analysis of this as well as the other mercury compounds is given in Table II.

TABLE II.—MERCURY DERIVATIVES.

Compound.	Analysis. Found.	Calculated.
2-Acetoxy-mercuri-3-nitro-4-hydroxy-diphenyl	N 2.82	2.95
$C_{14}H_{11}NO_6Hg$	Hg 41.6	42.4
Na salt 2-AcOHg-3NO_2-4HO-diphenyl	Hg 42.7	44.3
$C_{14}H_{10}NO_6HgNa$		
4-AcOHg-3,5-di-NO_2-2-HO-diphenyl	Hg 38.7	38.7
$C_{14}H_{10}N_2O_7Hg$		
4,6-DiAcOHg-3,5-di-NO_2-2HO-diphenyl	Hg 51.2	51.5
$C_{16}H_{12}N_2O_9Hg_2$		
3-NO_2-2-anhydro-Hg-5-acinitro-2-oxy-diphenyl	Hg 43.5	43.8
$C_{12}H_6N_2O_5Hg$	N 6.18; 6.05	6.10
Di-AcOHg-4′-NO_2-2-HO-diphenyl	Hg 53.2	54.9
$C_{16}H_{13}NO_7Hg_2$		
3-AcOHg-5-Br-2-HO-diphenyl	Hg 35.9	38.8
$C_{14}H_{11}O_3BrHg$		
5-AcOHg-2-phenyl-4-Br-phenoxy acetic acid	Hg 31.0	35.5
$C_{16}H_{13}O_5BrHg$		
HOHg-3,3′-diphenyl-5,5′-dibromo-phenolphthalein	Hg 26.6; 26.1	23.8
$C_{32}H_{20}O_6Br_2Hg$		
Di-AcOHg-3,3′-diphenyl-5,5′-dinitro-phenolphthalein	Hg 38.2	37.3
$C_{36}H_{24}O_{12}N_2Hg_2$		
AcOHg-3,3′-dinitro-phenolphthalein	Hg 32.8; 33.0	30.1
$C_{22}H_{14}N_2O_{10}Hg$		

3-NITRO-4-ANHYDRO-MERCURI-5-ACINITRO-2-OXY-DIPHENYL.

2.6 Gm. of 3,5-dinitro-2-hydroxy-diphenyl (5) were dissolved in 31 cc. *N* NaOH and heated to boiling. 3 Gm. of mercuric acetate dissolved in 50 cc. of water and 10 cc. glacial acetic acid were added and the mixture boiled and stirred for 20 hours. The bright orange product which had gradually become granular during the reaction was filtered off and washed with water, alcohol and ether. It dissolved in NaOH only on boiling and decomposed without melting above 300° C.

4′-NITRO-2-HYDROXY-DIPHENYL. (*a*) 4′-NITRO-2-AMINO-DIPHENYL.

This compound has previously been prepared (6) but the following directions give an improved yield.

167 Gm. conc. H_2SO_4 were cooled to 0° C. and 24 Gm. 2-amino-diphenyl added in small portions with good agitation. The solution was then cooled below 0° C. and a cooled mixture of 13 Gm. HNO_3 and 10 Gm. H_2SO_4 added at such a rate that the temperature remained below 0° C. Vigorous stirring was maintained during the addition and for 15–30 minutes afterward. The reaction mixture was then poured onto 200 Gm. cracked ice and allowed to stand for several hours before filtering off the 4′-nitro-2-amino-diphenyl-sulphate. It was not possible to wash the sulphate owing to rapid hydrolysis so the wet salt was suspended in water and the free base liberated by an excess of 10% NaOH. The bright orange base was recrystallized from alcohol and melted at 158–159° C. (corr.). Further confirmation of the position of the substituents was obtained by preparing the acetyl derivative m. p. 201° C. (corr.) and transforming the amine to 2-bromo-4′-nitro-diphenyl m. p. 81.5–82.5° C. (corr.). Scarborough and Waters state that 4′-ni-

tro-2-amino-diphenyl has m. p. 158° C. (corr.), 4′-nitro-2-acetamido diphenyl m. p. 199° C. (corr.), and 2-bromo-4′-nitro-diphenyl m. p. 82.5° C. (corr.).

(*b*) DIAZOTIZATION OF 2-AMINO-4′-NITRO-DIPHENYL.

18 Gm. 2-amino-4′-nitro-diphenyl were dissolved in the hot solution formed by adding 12 cc. H_2SO_4 to 120 cc. of water. The solution was heated to 90–95° C. and a solution of 5 Gm. $NaNO_2$ in 100 cc. water slowly added with stirring. The stirring was assisted by blowing in steam. When the evolution of nitrogen ceased the acid liquor was decanted, and the tarry residue extracted with boiling 2% NaOH. After treating with decolorizing carbon, the nitrophenol was precipitated by HCl and recrystallized from dilute alcohol. It formed white needles, m. p. 123–124° C., readily soluble in alcohol, ether and benzene.

Nitrogen: Found 6.2%. Calc. for $C_{12}H_9NO_3$ 6.5%.

5-BROMO-2-HYDROXY-DIPHENYL.

85 Gm. 2-hydroxy-diphenyl were dissolved in 100 cc. CS_2 or CCl_4 and the solution cooled to 0° C. Partial crystallization occurred but this appeared to have no effect on the bromination, the crystals rapidly dissolving during the early stages of the reaction. To the well-stirred, cooled solution, a solution of 80 Gm. bromine in 50 cc. CS_2 or CCl_4 was added, the reaction temperature being maintained below 5° C. by regulating the rate of addition. The solvent was then distilled off and the residue distilled under reduced pressure. B. p. 158–160/4 mm. The distillate formed a thick colorless oil which would not crystallize even on long standing. Yield—90%.

Bromine: Found 32.25%. Calc. for $C_{12}H_9OBr$ 32.13%.

2-PHENYL-4-BROMO-PHENOXY-ACETIC-ACID.

A solution of 5 Gm. of 5-bromo-2-hydroxy-diphenyl in 200 cc. *N* NaOH was boiled with 10 Gm. chloroacetic acid until the solution was neutral to litmus. It was then acidified and the gummy product dissolved in K_2CO_3 solution. After filtering the solution was acidified with dilute H_2SO_4 and the precipitate recrystallized from alcohol.

M. p.: 138–139° C. Yield—nearly quantitative.
C: Found 53.1%. Calcd. for $C_{14}H_{11}O_3Br$ 54.7%.
H: Found 3.8%. Calcd. for $C_{14}H_{11}O_3Br$ 3.6%.

ETHYL-2-PHENYL-4-BROMO-PHENOXY ACETATE.

24 Gm. of the above phenoxy acetic acid were esterified by boiling with 100 cc. absolute alcohol containing 4 Gm. HCl gas for $2^1/_2$ hours. The alcohol was then distilled off and the residual oil dissolved in ether and washed with Na_2CO_3 solution and water. After drying over $CaCl_2$ the ether was distilled off and the residue was analyzed without further purification, and mercurated.

C: Found 56.8%. Calcd. for $C_{16}H_{15}O_3Br$ 57.3%.
H: Found 4.6%. Calcd. for $C_{16}H_{15}O_3Br$ 4.5%.

2-PHENYL-4-BROMO-6-ACETOXY-MERCURI-PHENOXY-ACETIC ACID.

13 Gm. of the above ester were mercurated by the general method. The reaction mixture was then made strongly alkaline with NaOH and boiled to hydrolyze the ester. A heavy black precipitate which formed was filtered off and the filtrate acidified with acetic acid. The sticky precipitate was extracted with ether and the insoluble portion redissolved in Na_2CO_3, filtered and reprecipitated. It formed a white sandy powder, readily soluble in alkali and alkali carbonate solutions.

3,3′-DIPHENYL-PHENOL-PHTHALEIN.

10 Gm. phthalic anhydride, 36 Gm. 2-hydroxy-diphenyl and 8 Gm. conc. H_2SO_4 were heated for seven hours at 140° C. The purple melt was treated with water and boiled to remove any unreacted 2-hydroxy-diphenyl. The granular brown powder remaining was then dissolved in NaOH, filtered and reprecipitated with HCl and acetic acid. The precipitate was then dissolved in 100 cc. of alcohol, decolorized with charcoal and the alcohol solution diluted with 600

cc. of water. A small tarry precipitate was filtered off and the phthalein obtained from the filtrate by boiling out the alcohol. It formed a white fluffy powder. M. p. 234–235° C. An alkaline solution was violet-red, the color change from violet to colorless occurring between p_H 10.8–9.3.

C: Found 82.4. Calc. for $C_{32}H_{22}O_4$ 81.7%.
H: Found 5.05. Calc. for $C_{32}H_{22}O_4$ 4.7%.

3,3′-DIPHENYL-5,5′-DIBROMO-PHENOL-PHTHALEIN.

9.4 Gm. of the phthalein were suspended in 100 cc. of alcohol and 6.4 Gm. bromine added dropwise at 30–35° C. with stirring. The resulting red-colored solution was allowed to stand for some time and then poured into 500 cc. of water. The precipitate was filtered off, washed and recrystallized from dilute alcohol, m. p. 110–111° C. Yield—quantitative. An alkaline solution was deep blue with a slight red fluorescence by transmitted light. p_H range, colorless at 8.4 to red at 10.0.

Br: Found 24.98%. Calc. for $C_{32}H_{20}O_4Br_2$ 25.48%.

3,3′-DINITRO-5,5′-DIPHENYL-PHENOLPHTHALEIN.

9.5 Gm. 3,3′-diphenyl-phenolphthalein were suspended in 100 cc. glacial acetic acid and 3 cc. HNO_3 (sp. gr. 1.4) were added slowly with stirring. After warming on the water-bath for a few minutes the product was precipitated by adding 500 cc. water and recrystallized from alcohol. Yield—80–90%. Yellow needles, m. p. 135° C. after some softening at 115° C.

N: Found 5.08, 5.12%. Calc. for $C_{32}H_{20}N_2O_8$ 5.00%.

3,3′-DINITRO-PHENOL-PHTHALEIN.

20 Gm. of phenolphthalein were nitrated in exactly the same manner as the diphenyl phenolphthalein.

Yellow needles from dilute alcohol m. p. 110–111° C.

Yield—practically quantitative.

N: Found 6.59%. Calc. for $C_{20}H_{12}N_2O_8$ 6.78%.

SUMMARY.

A number of mercury derivatives of 2- and 4-hydroxy-diphenyl were prepared and their bactericidal properties investigated. The compounds mercurated were of two types, (*a*) in which a substituted hydroxy diphenyl was mercurated, (*b*) in which a phthalein prepared from hydroxy diphenyl was mercurated.

The mercury compounds have been shown to have considerable bactericidal activity.

REFERENCES.

(1) White, *J. A. C. S.*, 42 (1920), 2355.
(2) Greenbaum, *Am. J. Pharm.*, 102 (1930), 535.
(3) Whitmore, "Org. Compounds of Mercury," Chemical Catalog Co., N. Y. (1921).
(4) B. Latschinon, 6 (1872), 195.
(5) Borsche, *Ann.*, 312 (1900), 226.
(6) Scarborough and Waters, *J. C. S.*, 131 (1927), 95.

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United States Production of Coal-Tar Intermediates during 1932 totaled 218,143,000 pounds with sales of 96,960,000 pounds valued at $17,259,000, according to a United States Tariff Commission report. The 1931 output was 267,213,000 pounds with sales of 124,186 pounds, valued at $23,023,000.

A COMPARATIVE STUDY OF THE STABILITY OF EMULSIONS WITH VARIATION IN THE PROPORTION OF INGREDIENTS.*

BY LILLIAN MARY LANGEVIN.

DEFINITIONS OF TERMS.

An emulsion is a system containing two liquids that are immiscible, or practically so; one of which is dispersed in the form of globules in the other (1). The continuous or external medium is termed the dispersion phase (or dispersing phase), and the dispersed globules are called the internal or dispersed phase (or disperse phase) (2).

In general, there are two kinds of emulsions; namely, those that occur naturally and those that are produced artificially. Natural emulsions include animal emulsions and plant emulsions. Artificial emulsions may be produced by mixing two immiscible liquids. Theoretically, it should be possible to make two types of emulsions from any two given immiscible liquids. Assuming that oil and water are the two given liquids, one emulsion should correspond to the "oil-in-water" (o/w) type and the other should correspond to the "water-in-oil" (w/o) type. However, Clayton (3) states that if only *pure water* and *pure oil* are used only a single type of emulsion can be produced and that is a dilute oil-in-water (o/w) emulsion. A second class of emulsions exists which includes concentrated and more complex emulsions of both the oil-in-water and the water-in-oil type. The stability or permanence of this class depends upon the presence of a third substance called an emulsifying agent or emulsifier. These concentrated and complex emulsions possess considerable commercial and industrial importance, while the dilute, simple emulsions of oil-in-water have very little practical significance.

If two pure immiscible liquids are shaken together, both liquids are divided into globules and become intermixed. Upon standing, the globules of the respective liquids unite and separation into two distinct layers occurs. When a third substance, called an emulsifier, is included in a system consisting of oil and water it tends to stabilize the system, and to form a permanent emulsion. An emulsifying agent that is more readily wetted by water than by oil will form an oil-in-water emulsion; one that is more readily wetted by oil, a water-in-oil emulsion (4). Many substances have been used as emulsifiers. These include soaps, egg-yolk, acacia, tragacanth, Irish moss, proteins, carbon, clay and many other finely divided substances.

THEORIES OF EMULSIFICATION.

The development of Colloidal Chemistry has given rise to several theories of emulsification. Ostwald (5) in 1910, formulated the "Phase-Volume Theory" which was based upon the theory of piled spherical balls. This theory is no longer generally accepted. A second theory is known as the "viscosity theory." Early investigators recognized the fact that the viscosity of the external phase probably had some influence on the stability of emulsions (6). Clayton states that "the majority of investigators to-day accept the conclusion that *viscosity aids emulsifi-*

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cation solely by virtue of the hindrance offered to coalescence of the dispersed globules, and is not the *cause* of emulsification."

In 1917, Fischer (7) advocated the "hydration theory" of emulsions and emulsification. The "surface tension theory" was the forerunner of the "adsorption film theory" which is quite generally accepted to-day. Bancroft (8) formulated the "adsorption film theory" in 1913. He conceived the idea that the protective film surrounding the dispersed phase was a *separate phase,* which was wetted on one side by the oil phase and on the other side by the water phase and which had different surface tensions on the two sides. The type of emulsion produced depends upon the relative surface tension at the interfaces. The side of the intervening film which has the greater surface tension tends to become concave and enclose the liquid on that side, and the other liquid of lower surface tension tends to become the outer phase, since the tendency in any system is to assume the most stable condition, which is that which exists when the least surface energy is expended.

HISTORY OF PHARMACEUTICAL EMULSIONS.

Emulsions have been used medicinally for a very long period of time. H. Schelenz (9) says that Pliny described a drink made of almonds and honey that may have been the original almond emulsion. The earliest reference that he finds to the word emulsion is "de Emulsionibus" in Schroeder's Pharmacopœia of the seventeenth century. Oil emulsions were first described by Baumé.

The early pharmaceutical literature of the United States makes mention of emulsions. This early literature from about 1830 up until about 1865 was concerned largely with the publication of formulas for the production of emulsions.

During the forty-year period from about 1860 to 1900 investigations were made relative to methods of emulsification, to the kind of emulsifier, and to the proportions of ingredients which should be used in emulsions. The "bottle method," the "English method" and the "Continental method" of emulsification were advocated. Many different emulsifying agents were proposed. There appears to have been a great diversity of opinion regarding the proportion of ingredients to be used in emulsions.

Pharmaceutical literature indicates that emulsions were first produced upon a large scale for commercial distribution about 1900.

EXPERIMENTAL STUDY AND RESULTS.

The object of this experiment was twofold; *first,* to determine the effect of dilution upon the stability of emulsions of oils of animal and vegetable origin which are used pharmaceutically; and, *second,* to determine the limits of emulsification or emulsibility of these oils when variation in proportion of ingredients occurred, and incidentally, to determine whether or not the proportions of ingredients, which are recommended by the present United States Pharmacopœia and National Formulary for the preparation of emulsions of fixed oils, are optimum.

It should be said, in the beginning, that this problem was approached from the practical standpoint. An attempt was made to simulate the conditions which occur in the average drug store. The materials and apparatus used were, for the most part, similar to those found in drug stores; and, the manipulation was as

uniform as possible. The acacia was weighed on a torsion balance and the water and oils were measured in cylindrical or conical graduates. These measurements were made in this manner so that the conditions of the experiment might be duplicated in the average drug store where, it is hoped, this work may prove to be of some practical value.

The materials used were purchased on the open market in quantities sufficient to run the entire series of experiments so as to insure uniformity of ingredients. The oils included expressed oil of almond, castor oil, cod liver oil, cottonseed oil, raw linseed oil, olive oil and sesame oil. Acacia was chosen as the emulsifying agent since it is most commonly used. The specific gravities of the oils were checked using both the pycnometer and the Mohr-Westphal balance. Relative or specific viscosity was determined, the Saybolt viscosimeter being used. These physical constants appear in Table I.

In studying the effect of dilution upon pharmaceutical emulsions, large quantities of primary emulsions were prepared. Enough primary emulsion was made to supply the base for a single series of dilutions, separate primary emulsions were prepared for each series. Duplicate series of each oil were run, the Continental or 1:2:4 (A:W:O) method of emulsification was used. Twelve hundred cc. of a given oil which contained 0.5% of dissolved thymol (this was used as a preservative) were thoroughly mixed with 300 Gm. of acacia in a large wedgewood mortar, then 600 cc. of water were dashed in at once, and the mixture triturated until a thick, viscous, homogeneous, creamy emulsion resulted.

Dilutions of these primary emulsions were made. In order to not lose any of the primary emulsion by pouring from one container to another, the required amount of primary emulsion was measured directly into graduated 8-ounce prescription bottles. The required amount of emulsion was determined in the following manner. For example, it was necessary to make a dilution of primary emulsion of cod liver oil, which when finished would contain 10 per cent of oil. The factor used in determining the quantity of primary emulsion necessary in any given dilution was determined in the following way. One hundred cc. of oil were thoroughly mixed with 25 Gm. of acacia in a graduated 240-cc. bottle. Then 50 cc. of water were added and the mixture was shaken until emulsification or at least uniform mixing occurred. The mixture was allowed to settle until air bubbles had escaped and then the quantity of emulsion measured. In the case of cod liver oil, 100 cc. of oil produced 168.75 cc. of emulsion. The resulting factor was 168.75/ 100 or 1.6875 in this case. Then if a 10 per cent emulsion of cod liver oil was required, 24 cc. of oil would be required. The amount of primary emulsion corresponding to this would be 24 times the factor 1.6875 or 40.50 cc. The primary emulsion was poured into the graduated bottle up to the indicated mark.. Dilution was made by adding the required water in 5-cc. portions; thorough mixing occurred after each addition. The finished emulsions were stored at room temperature.

These dilute emulsions were examined daily over a period of 30 days for signs of cracking, decomposition and other changes that might occur. (By cracking is meant the complete separation of the mixture into two distinct layers, an oil layer and a water layer.) There were no cases of cracked emulsions. However, emulsions which contained 30 per cent or less of oil, usually showed a separation in the form of a supernatant, creamy layer which was readily reincorporated by

shaking. The number of cubic centimeters in this creamy layer was measured daily. This was done by measuring the liquid upon the side of the graduated bottle. Then, the emulsions were thoroughly shaken up and allowed to stand until the following day. At the end of the 30-day period, the average number of cubic centimeters of separation was calculated and converted into percentage.

Decomposition occurred in the castor oil emulsions which developed rancidity after about the fourth day. Considerable gas was evolved and in several cases sufficient pressure was developed to force the corks from the bottles. A decided odor of butyric acid was present. In emulsions ranging from 25 to 40 per cent a dark lumpy-looking layer formed at the bottom of the bottle. This was probably due to decomposition products.

Some of the cottonseed oil emulsions, while apparently not rancid, developed a "slimy," "buttery" appearance in the supernatant layer and toward the end of the period it was impossible to mix this layer with the rest of the mixture.

The more dilute emulsions of expressed oil of almond showed a double layer, the upper one having a very oily appearance.

Several emulsions in the various series showed a tendency to form lumps which could be shaken out easily.

After the 30-day period, the specific viscosity of these emulsions was determined so far as it was possible to run them through the viscosimeter. These values may be found in Table II.

Table III indicates the percentage of separation of these emulsions.

An effort was made to determine the limits of emulsibility of these seven oils when varying proportions of ingredients were used. The order of mixing used was that of the Continental method. Starting with the 1:2:4 proportion, three series of emulsions were made, varying acacia, water and oil, respectively. In each case, the variation amounted to a progressive increase or decrease equal to 20 per cent of the original proportion of the variable ingredient. For example, in a series in which water was varied, the proportions were 1:4:4, 1:(3.6):4, 1:(3.2):4, 1:(2.8):4, 1:(2.4):4, 1:2:4, 1:(1.6):4, 1:(1.2):4, 1:(0.8):4, 1:(0.4):4. Small portions of these emulsions were prepared, averaging about 20 cc.–25 cc. of finished emulsion. The smallest amount of liquid used was never less than 5 cc. When an emulsion resulted at the first trial it was not repeated. When emulsions failed at the first attempt, three or more trials were made, unless it was obvious that an emulsion could not be formed, as for example, when so great a bulk of acacia was present that the system could not be manipulated.

It was found that emulsibility was not limited to any given proportion of ingredients, but rather that it was possible to produce an excellent grade of emulsions over a small range, and emulsions of decreasing quality with increasing variation in proportions of ingredients beyond that range.

Since emulsions were produced over a considerable range and the limit of emulsibility was not sharp, the diameter of the oil globules in the various emulsions was determined microscopically, in the effort to see if they might give a numerical criterion of quality.

The procedure was as follows. A graduated eyepiece was calibrated to read in microns. High power was used for the determinations. Three slides were made from each emulsion, similar to the way in which smears are made in bac-

teriology. The diameters of ten oil globules from each slide were recorded, those globules which touched the 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5 and 5.0 marks on the scale were arbitrarily selected. The average diameters are listed in Tables IV, V and VI.

Table IV which shows the changes in proportion of acacia tends to show that an increase in acacia is accompanied by a reduction in the size of oil globules. An increase in the proportion of acacia is limited by the thickness developed in the mixtures containing high proportions of acacia, rendering the manipulation of the system impossible. A decrease in acacia beyond about 1.0 part or 0.8 part tends to cause a rapid increase in globule size and lack of emulsibility.

When the proportion of water was varied an increase in water resulted in an increase in the size of the oil globules. If less than 1.6 parts of water were used the mixture was a thick gummy mass, in most cases almost doughy. Upon the addition of more water, a fairly good emulsion generally resulted. Greater quantities than about 2.5 parts of water resulted in emulsions which creamed rapidly (Table V).

Emulsions made with variations in the proportions of oil showed that the most stable emulsions resulted when from 2.0 to 4.0 parts of oil were used (Table VI)

TABLE I.—SHOWING SPECIFIC GRAVITY AND RELATIVE VISCOSITY OF THE OILS USED IN PREPARING EMULSIONS.

Oil.	Sp. Gr. (25° C.).	Relative Viscosity (25° C.).
Expressed oil of almond	0.9131	16.84
Castor oil	0.9592	104.04
Cod liver oil	0.9210	8.35
Cottonseed oil	0.9199	16.89
Raw linseed oil	0.9266	12.21
Olive oil	0.9115	11.37
Sesame oil	0.9196	10.53

TABLE II.—SHOWING SPECIFIC VISCOSITY OF EMULSIONS AT THE END OF THE 30-DAY PERIOD.

% of Oil.	Expressed Oil of Almond.	Castor Oil.	Cod Liver Oil.	Cottonseed Oil.
5	1.11	1.14	1.30	*d*
10	1.22	1.17	1.40	*d*
15	1.34	*d*	1.67	1.46
20	1.61	1.49	2.03	1.92
25	1.93	2.16	3.02	2.65
30	2.90	3.37	4.81	4.28
35	5.98	5.54	..	..

% of Oil.	Raw Linseed Oil.	Olive Oil.	Sesame Oil.
5	1.07	1.25	1.15
10	1.17	1.40	1.28
15	1.38	1.57	1.51
20	1.82	2.14	1.92
25	2.53	3.21	2.91
30	4.23	5.05	4.27
35	..	..	..

d signifies decomposition or rancidity.

TABLE III.—SHOWING THE AVERAGE PERCENTAGE OF SEPARATION IN EMULSIONS OF VARYING OIL PERCENTAGE.

Oil.	Series.	% of Oil in the Finished Emulsion. 5%.	10%.	15%.	20%.	25%.
Expressed oil of almond	A	10.46	15.46	21.29	26.50	31.83
	B	10.71	15.96	21.14	27.31	30.54
Castor oil	A	10.86	15.33	21.54	26.92	31.38
	B	10.68	15.44	20.92	23.35	*
Cod liver oil	A	12.42	15.46	20.04	18.13	*
	B	11.63	14.48	16.79	16.54	*
Cottonseed oil	A	10.72	17.46	22.51	26.21	25.54
	B	12.03	17.63	22.53	24.13	*
Linseed oil	A	10.33	13.38	16.79	17.42	15.95
	B	12.63	14.01	17.04	17.46	17.04
Olive oil	A	10.82	17.23	20.63	23.88	*
	B	10.83	17.43	20.75	24.89	*
Sesame oil	A	10.92	16.83	22.99	30.43	35.54
	B	10.71	16.58	22.67	28.71	*

Oil.	Series.	% of Oil in the Finished Emulsion. 30%.	35%.	40%.	45%.	50%.	55%.
Expressed oil of almond	A	36.77	43.46	59.04	81.00	*	*
	B	37.88	47.42	59.13	87.46	*	*
Castor oil	A	*	*	*	*	*	*
	B	*	*	*	*	*	*
Cod liver oil	A	*	*	*	*	*	*
	B	*	*	*	*	*	*
Cottonseed oil	A	*	*	*	*	*	*
	B	*	*	*	*	*	*
Linseed oil	A	18.29	*	*	*	*	*
	B	31.21	*	*	*	*	*
Olive oil	A	*	*	*	*	*	*
	B	*	*	*	*	*	*
Sesame oil	A	*	*	*	*	*	*
	B	*	*	*	*	*	*

* No separation occurred within the 30-day period.

TABLE IV.—SHOWING THE AVERAGE DIAMETER IN MICRONS OF OIL GLOBULES IN EMULSIONS WHICH HAVE VARYING PROPORTIONS OF ACACIA.

Prop. of Acacia.	Expressed Oil of Almond.	Castor Oil.	Cod Liver Oil.	Cottonseed Oil.
2.0	**	3.0	2.4	4.2
1.8	3.8	2.6	4.1	3.3
1.6	3.5	2.5	3.2	3.4
1.4	4.7	3.7	4.6	3.5
1.2	4.1	2.6	5.8	4.3
1.0	5.0	4.2	4.4	3.4
0.8	5.5	5.2	6.0	5.7
0.6	8.1	6.5	10.3	7.9
0.4	10.6	**	**	8.0

Prop. of Acacia.	Raw Linseed Oil.	Olive Oil.	Sesame Oil.
2.0	4.8	4.4	**
1.8	5.6	3.8	4.6
1.6	5.4	3.9	5.2
1.4	4.7	4.9	5.2

1.2	6.3	4.1	5.4
1.0	6.2	3.6	2.9
0.8	5.5	5.7	5.8
0.6	11.6	14.8	7.9
0.4	14.8	14.7	22.7

** No emulsification obtained.

TABLE V.—SHOWING THE AVERAGE DIAMETER IN MICRONS OF OIL GLOBULES IN EMULSIONS WHICH HAVE VARYING PROPORTIONS OF WATER.

Prop. of Water.	Expressed Oil of Almond.	Castor Oil.	Cod Liver Oil.	Cottonseed Oil.
4.0	**	**	17.9	16.6
3.6	10.0	15.2	17.3	12.0
3.2	9.5	14.9	12.3	8.6
2.8	10.4	8.3	8.6	6.0
2.4	6.3	4.8	6.5	4.6
2.0	5.0	4.2	4.4	3.4
1.6	5.4	3.5	4.2	3.8
1.2	**	**	**	**

Prop. of Water.	Raw Linseed Oil.	Olive Oil.	Sesame Oil.
4.0	**	**	**
3.6	8.8	19.2	18.1
3.2	8.7	11.8	9.2
2.8	7.2	7.4	5.4
2.4	5.7	4.5	6.5
2.0	6.2	3.6	2.9
1.6	7.9	3.0	3.9
1.2	**	**	**

** No emulsification obtained.

TABLE VI.—SHOWING THE AVERAGE DIAMETER IN MICRONS OF OIL GLOBULES IN EMULSIONS WHICH HAVE VARYING PROPORTIONS OF OIL.

Prop. of Oil.	Expressed Oil of Almond.	Castor Oil.	Cod Liver Oil.	Cottonseed Oil.
6.4	**	5.0	**	**
5.6	5.8	4.6	**	4.5
4.8	5.5	4.2	4.8	4.9
4.0	5.0	4.2	4.4	3.4
3.2	4.1	3.1	3.2	4.0
2.4	5.0	3.9	3.7	4.2
1.6	6.4	4.5	4.6	4.9
0.8	11.3	6.6	10.0	9.9

Prop. of Oil.	Raw Linseed Oil.	Olive Oil.	Sesame Oil.
6.4	**	**	**
5.6	7.4	5.0	**
4.8	5.5	5.9	7.1
4.0	6.2	3.6	2.9
3.2	4.6	4.1	4.7
2.4	4.8	4.3	4.6
1.6	4.4	5.9	7.4
0.8	6.0	8.1	10.0

** No emulsification obtained.

SUMMARY AND CONCLUSIONS.

1. Dilutions of primary emulsions of expressed oil of almond, castor oil, cod liver oil, cottonseed oil, raw linseed oil, olive oil and sesame oil were prepared so that the finished emulsions contained oil percentages varying from 5 to 55 per cent. In no case, did cracking or breaking of the emulsion occur. "Creaming" occurred in emulsions containing 30 per cent or more of oil, but this cream layer was readily reincorporated by agitation.

2. A change in the variation of proportion of ingredients in emulsions of the oils named above resulted in the following conclusions:

(*a*) An increase in the proportion of acacia is accompanied by a decrease in the size of the oil globules and vice versa.

(*b*) An increase in the proportion of water results in an increase in the size of dispersed oil globules.

(*c*) Emulsions containing from 2.0 to 4.0 parts of oil had the smallest oil globules.

(*d*) It appears probable that the smaller the range in variation of size of oil globules the more stable the emulsion.

(*e*) Emulsions of fixed oils may be prepared with a much wider range in variation in proportion of ingredients than the 1:2:4 rule would indicate. The results of this experiment showed that emulsions made according to the 1:2:4 rule were not always optimum; however, satisfactory emulsions of fixed oils should result when these proportions of ingredients are used.

BIBLIOGRAPHY.

(1) W. Clayton, "Theory of Emulsions," 2nd Edition (1928), page 1.
(2) Kruyt and von Klooster, "Colloids," 2nd Edition (1930), page 7.
(3) W. Clayton, "Theory," page 2.
(4) *Ibid.*, page 25.
(5) *Kolloid-Z.*, 6 (1910), 103; 7 (1910), 64; through Clayton, "Theory," page 45.
(6) W. Clayton, "Colloidal Aspects of Food Chemistry and Technology" (1932), page 165.
(7) Fischer and Hooker, "Fats and Fatty Degeneration" (N. Y., 1917), page 5; through Clayton, "Theory," page 60.
(8) *J. Phys. Chem.*, 17 (1913), 514–518; through Clayton, "Theory," page 120.
(9) YEAR BOOK, A. PH. A., Vol. 10 (1921), 81; *Schweiz. Apoth.-Ztg.*, 59 (1921), 657.

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DECEPTIVE LITERATURE OF 50 YEARS AGO.

The Chemist and Druggist, of April 14, 1883, contains this paragraph—"Seldom has a richer specimen of our omniscient journalism been printed than this choice sentence: 'It has been stated recently that in the manufacture of soda water, marble dust and oil of vitriol are largely used; and although there may be exaggeration in this, as there generally is in assertions of a wholesale character, still the imputation is one which the great brewers should be anxious to refute, as indeed they did successfully refute the charge of using aconite instead of hops in the manufacture of bitter beer.'" This is not so very different from recent literature. "Let it be the ardent desire of every pharmacist that pharmacy and pharmacists will maintain their dignity and professional standards."

THE EXTRACTION AND ASSAY OF CRUDE ERGOT.*

BY MARVIN R. THOMPSON (1) (*Continued from page 1141, November 1932*).

EXTRACTION BY PROCESS OF U. S. P. X.

The studies herein described were designed to shed light upon serious discrepancies in results obtained in the assay of crude ergot by experienced workers, which have from time to time come to the writer's attention. Also, to reveal, if possible, the cause of the all too frequent inability of pharmaceutical manufacturers to obtain an amount of standardized Fluidextract of Ergot in agreement with the previous assay of a small sample of the crude ergot involved. The fact that the yield of standardized product on different occasions has been observed to exceed as well as fall short of the amount predicted by previous assay of the particular crude drug involved, would at first cause one to suspect the accuracy of the assay method as the main cause of discrepancies. On a number of occasions, however, extremely critical check assays by all three of the most accurate of known methods (Rabbit Uterus, Colorimetric and Cock's Comb) left no doubt but that some discrepancies were of a magnitude greater than could possibly be accounted for by experimental error in the assays. Since the present U. S. P. requires the conversion of crude ergot into a Fluidextract of Ergot by a specified Type Process "B" for the assay, it appeared distinctly possible that the observed discrepancies might be accounted for by a difference in efficiency between "commercial scale" and "laboratory scale" preparation of the Fluidextract. A critical study of the official Type Process "B" was, therefore, undertaken.

The study yielding the results herein reported was conducted upon twelve different lots of crude ergot, although experience with ergot during five years has provided many more observations intimately related to this problem. Six of the lots selected were of poor to fair quality, while the other six were of good quality. These six lots were converted to fluidextracts by the official type process "B" of the U. S. P., and the "reserve" as well as the "exhaust" percolates were subjected to critical assay for alkaloidal activity by the Rabbit Uterus method according to the technique described in the preceding article of this series. After assay of the "reserve" and "exhaust" percolates, the "exhaust" percolates were concentrated as directed by the U. S. P. and incorporated in the "reserve" portion, adjusting the volume to 100 cc. (from 100 Gm. of drug) in all cases. These finished products were then likewise assayed. Ergotoxine Ethanesulphonate was used as the standard in these assays.

It is important to note that all six lots were subjected as closely as possible to the same type of treatment, *i. e.*, all lots were reduced to powders of equal fineness, percolators of the same size and shape were used, percolation was carried on very slowly and at identical rates for all, the same moderate temperature was applied to all during concentration of "exhaust" percolates, etc.

TESTS FOR EXHAUSTION OF THE DRUG.

These chemical tests have been developed in order to avoid the necessity of routinely testing for exhaustion by physiological methods. Their sensitivity and

* Scientific Section, A. PH. A., Toronto meeting, 1932.

reliability have been carefully checked physiologically and approved for the intended practical purpose for which they were designed.

Percolation was in all cases carried to the same degree of exhaustion. Absence of color in the percolates was utilized merely as a rough criterion as to completeness of extraction. The following two chemical tests were used routinely in every case for proving exhaustion, as follows. (These tests were not ordinarily applied until percolate was nearly colorless.)

Test (*a*). Approximately 4 cc. of the issuing percolate is diluted threefold with a saturated aqueous solution of sodium bicarbonate. Failure to develop precipitate, turbidity or faint opalescence during one hour shows that extraction is sufficiently complete for practical purposes.

Test (*b*). This test is somewhat less sensitive than (*a*). Approximately 4 cc. of the issuing percolate is diluted twofold with water and made slightly but distinctly alkaline to litmus by the cautious addition of 1% ammonia water. Failure to develop precipitate, turbidity or faint opalescence during one hour shows that increasing the volume of the percolate by further extraction would not be justifiable.

These tests are also reliable and serviceable in the event tests are desired upon percolates containing some color, *i. e.*, before the color has disappeared from the percolate. If color is present, no other indicator is necessary in applying test (*b*), since this color changes upon being made faintly alkaline.

The results obtained in the extraction experiments are recorded in the following Table I.

TABLE I.

The proportions of ergot alkaloidal activity appearing in the "Reserve Portion," the "Exhaust Percolate," and also comparing the alkaloidal activity of the Type Process "B" Fluidextract with that of a straight quantitative percolate. All assays by the Epinephrine-Inhibition method. Alkaloidal content expressed in terms of Ergotoxine Ethanesulphonate.* 100-Gm. samples of crude ergot used in each case.

Crude Drug.	Amt. of Alkaloid Present in the 85 Cc. Reserve Portion. Mg.	Per Cent of Total Alkaloid Present in Drug (Approx.).	Additional Vol. of Percolate Obtained to Exhaust the Drug, Cc.	Amt. of Alkaloid Present in the Total Exhaust Percolate. Mg.	Per Cent of Total Alkaloid Present in Drug.	Total Amt. of Alkaloid Present in Drug, Mg. (Calculated), Reserve plus Exhaust.	Total Alkaloid in 100 Cc. F. E. by Type Process "B," Mg.	Per Cent Total Alkaloid Lost by Concentration of Exhaust Percolate of Type Process "B" (Approx.).
1	33.2	55	415	27.2	45	60.4	46.5	23%
2	13.77	43	465	18.03	57	31.8	20.2	36%
3	50.97	58	515	37.23	42	88.2	62.7	28%
4	135.8	63	515	79.4	37	215.2	170.2	20%
5	92.02	52	565	85.98	48	178.0	108.5	39%
6	117.8	60	465	78.2	40	196.0	133.0	32%

* Generously supplied by Dr. C. S. Leonard, Burroughs, Wellcome & Co.

DISCUSSION OF TABLE I.

The results tabulated above are uniformly significant in showing that, in spite of most careful attention to details shown by experience to influence efficiency in extraction of drugs, the "reserve portion" cannot be expected to contain significantly more than one-half of the total activity of the drug, thus essentially confirming the experiments of Wokes and Elphick (2). It logically follows, therefore, that the remainder of the activity must be contained in the "exhaust percolate," which, the results show, attains a considerable volume before extraction is reasonably complete. From the standpoint of accurate bioassays of crude ergot, and also from the standpoint of commercial extraction of ergot, it is highly significant that concentrating the exhaust percolate for incorporation into the reserve portion results in a loss of activity that is great and

likewise considerably variable. Other experiments conducted in this laboratory have shown that the employment of partial vacuum in the concentration of the exhaust percolate does not avoid the loss of considerable activity. Similarly, the use of a hot air blast to affect the concentration was found to be attended by a loss of considerable activity. The writer has been unable to find any practical method of concentrating such hydro-alcoholic ergot percolates which could be carried out without the danger of losing an objectionable amount of the activity.

The above results make it readily apparent that the procedure at present specified by the U. S. P. for the assay of crude ergot cannot possibly reflect the true potency of the drug, even though the methods of testing the resulting fluidextract were 100 per cent accurate. Because of the loss of activity incurred in the procedure of concentrating the large volume of "exhaust" percolate, the most accurate assay possible must necessarily reveal a potency approximately 20 to 30% lower than was actually present or extractable from the drug. It is important to point out that the loss so incurred cannot be assumed to be even reasonably constant, for a number of reasons. Different samples of ergot vary greatly with respect to ease of extraction, some being well extracted by a 1 to 4 percolate, while others require percolation to the extent of 1 to 10. Aside from the natural variations in ergot, such factors as size and uniformity of particles of the ground drug, completeness of de-fatting, height of the column of drug in the percolator, amount of packing of drug, temperature during entire extraction procedure, time of maceration and rate of percolation are vitally concerned in extraction efficiency. Since certain of these factors cannot be precisely controlled, it is obvious that considerable variation in extraction efficiency as well as in concentration technique would occur from laboratory to laboratory, due in part to the personal equation of the operator. Consequently, the proportions of activity obtained, respectively, in the "reserve" and "exhaust" percolates are subject to considerable variation. Generally speaking, the greater the proportion of activity contained in the "exhaust" percolate to be concentrated for incorporation into the "reserve" portion, the greater is the loss of activity sustained. The converse is also true, *i. e.*, the greater the proportion of the total activity contained in the "reserve" portion, the less will be the loss sustained by concentration of the "exhaust" percolate.

It will be apparent from the above, that it is virtually impossible, at least extremely improbable, for two or more different workers to obtain fluidextracts of identical potency from different portions of the same lot of ergot using the Type Process "B" specified by U. S. P. X. Even assuming that the several workers would attain absolute accuracy in assaying their respective fluidextracts, the results would necessarily be variable and in all cases show a potency considerably lower than that actually present in the drug under examination.

The failure of the procedure specified by the present U. S. P. to provide for the appearance of the total amount of activity of the drug in the liquid to be subjected to assay, was responsible for an investigation of other possible extraction procedures with the hope of developing one which would be more dependable in providing for the appearance, in the liquid extract, of the total amount of activity contained in the crude drug, thereby eliminating at least this serious source of error in assaying crude ergot.

The results of Table I suggested a fairly obvious course to follow for affecting such a dependable quantitative extraction of the sample to be assayed. Since the observed variable loss in activity was sustained only in the concentration of the "exhaust" percolate, it seemed certain that the direct assay of the total unconcentrated quantitative percolate would yield a true estimate of the activity contained in the crude drug. In carrying out such a simple quantitative percolation, it is obviously advantageous to obtain the total activity of the drug in as small a volume of percolate as possible, and at the same time, if possible, to have the nature of this quantitative percolate such that it would lend itself to direct assay without the necessity of subjecting it to chemical procedure prior to such assay.

Experience has shown that a menstruum consisting of approximately equal parts of alcohol and water is the most satisfactory for insuring an efficient extraction of ergot and at the same time providing for a percolate which could be assayed directly without further manipulation. It is now generally agreed that the extraction efficiency is enhanced somewhat by the addition of a small amount of acid to this menstruum. In an earlier series of communications (10), the writer emphasized the importance of the use of hydrochloric acid in the menstruum, partly because of a moderately favorable influence upon extraction efficiency, but mostly because of the

well-known work of Swanson which definitely showed that an appreciably acid p_H favored the stability of the finished fluidextract. Further reference to p_H and stability will be discussed later.

The fact that such straight quantitative percolates attain great volumes, causing the alkaloidal concentration of the usual run of samples to fall in the low range of 0.005 to 0.05 per cent in terms of ergotoxine, bars the accurate use of the official Cock's Comb method or any of its modifications. The Isolated Rabbit Uterus method, as described in the preceding communication, provides ample sensitivity for this purpose and was consequently the method of choice. Greatly excessive acidity in the test percolate is highly objectionable in the application of this method, as will be shown in a later report from this laboratory. Since added acidity exerts only a moderate influence on extraction efficiency, and since the stability of the percolate is not a disturbing factor in this assay procedure, there is no reason for employing excessive amounts of acid in the menstruum.

A considerable number of experiments has led to preference for the following procedure as a method for the assay of crude ergot, definitely more reliable than the method at present specified by U. S. P. X.

METHOD.

(*a*) *Assay Sample.*—It is extremely important to use all possible care in securing an assay sample that is representative of the lot in question. Crude ergot is invariably imported or shipped in bags. The potency shown by samples from different bags of the same shipment, or even samples taken from different parts of the same bag, has been found on a number of occasions to vary considerably. The writer is convinced that it is not advisable to conduct an assay upon a representative sample weighing less than 50 Gm., while the extraction of a 100-Gm. sample is preferable.

(*b*) *Extraction Procedure.*—The drug is ground in the usual manner and sifted in a No. 30 sieve, returning portions remaining in the sieve to the mill, until all has passed through. The powder is then thoroughly mixed, and the accurately weighed assay portion of the powder is transferred without packing to a properly prepared glass percolator. The percolator should be of such a size and shape that the column of drug attains a height of at least five times the average diameter of the percolator while at the same time leaving space for menstruum above the drug. Within reasonable limits, the higher the column of drug, the greater is the extraction efficiency. The powder is then de-fatted as directed in U. S. P. X, and finally freed from the benzine. The de-fatted powder is then moistened with a sufficient quantity of a menstruum consisting of 2 per cent by volume of Hydrochloric Acid, U. S. P., in diluted alcohol (equal parts by volume of alcohol and water) to render it evenly and distinctly damp. It is then again transferred to the percolator, lightly shaken down but not packed. More of the same acidified menstruum is added, maintaining a layer of liquid above the drug, until the liquid reaches the lower orifice. The outlet is then closed and the whole allowed to stand for 12 hours or over night. After this maceration period, percolation is allowed to proceed at a very slow rate, using diluted alcohol as menstruum until the color is practically absent from the issuing percolate and the issuing percolate proves negative to the "Tests for Exhaustion" given above.

The volume of percolate obtained is then noted and the liquid is assayed by the Isolated Rabbit Uterus method, expressing the potency of the drug, after appropriate calculation, in terms of a suitable standard.

If it is preferred, the percolate likewise lends itself to assay by the Smith Colorimetric method or any of its several modifications.

As previously stated, the low concentration of alkaloidal activity in such quantitative percolates precludes the possibility of applying the official Cock's Comb method with any acceptable degree of accuracy.

The following Table II shows very clearly that a fluidextract prepared by Type Process "B" does not contain the full amount of activity actually contained in the drug sample, confirming the results of Table I. This table also shows the greater assay accuracy provided by the extraction method described above.

In explanation of Table II, it should be pointed out that the six samples of crude ergot involved were the same samples under examination in Table I. The identification numbers of the drug samples correspond in the two tables. The results shown in Table II are self-explana-

TABLE II.—THE POTENCY OF CRUDE ERGOT ASSAYED AS THE U. S. P. X FLUIDEXTRACT, AS COMPARED TO THE POTENCY REVEALED WHEN A "QUANTITATIVE PERCOLATE"** IS ASSAYED.

Crude Drug No.	Total Alkaloid* from 100-Gm. Drug after Conversion to U. S. P. X Fluidextract, Mg.	Total Alkaloid* in "Quantitative Percolate"** from 100-Gm. Drug, Mg.	Vol. of Quantitative Percolate from 100-Gm. Drug, Cc.
1	46.5	64.7	650
2	20.2	34.1	650
3	62.7	89.7	650
4	170.2	209.3	800
5	108.5	175.5	700
6	133.0	203.3	750

* In terms of Ergotoxine Ethanesulphonate.

** Prepared by the process just described.

tory. A source of serious error in the present U. S. P. X procedure for assaying crude ergot is clearly revealed. By adding the possible error caused by the present official extraction procedure to the possible error inherent with available assay methods, the discrepancies encountered in the assay of crude ergot by the same or different workers are readily accounted for. The first source of error can be eliminated in a very practical manner by employing the simple extraction technique just described. A further advantage over the U. S. P. X procedure lies in the fact that the concentration of "exhaust" percolate is eliminated, thereby saving time and expense.

The quantitative percolate obtained by the above procedure does not, of course, constitute an acceptable therapeutic ergot preparation. The potency represents that of a tincture rather than a fluidextract, and this would necessitate a prohibitively large therapeutic dose. A more efficient method of preparing a 1:1 fluidextract than is provided by the U. S. P. X requirements would obviously be desirable from the manufacturer's standpoint for economic reasons alone. A consideration of this problem follows.

AN IMPROVED METHOD FOR PREPARING FLUIDEXTRACT OF ERGOT, U. S. P.

The preceding experiments clearly show that the active principles of ergot are partially destroyed by the moderate heat necessary for concentration of the "exhaust" percolate in the Type Process "B" at present specified by the U. S. P. It is obvious, therefore, that a method of preparation not involving the use of heat would avoid the loss of activity sustained in carrying out the present official method.

The "Fractional" or "Divided Percolation" method, designated as "Type Process C," of the U. S. P. X, page 160, is recommended for drugs containing constituents which are injured by heat. This entire procedure is carried out at room temperature, no concentration of weak percolates being necessary.

A series of experiments were undertaken to determine the relative applicability of Type Process "C" as compared to Type Process "B." The same single menstruum was used throughout for each process, and consisted of 1% of U. S. P. Hydrochloric Acid in diluted alcohol (equal vols. of water and alcohol). This amount of acid was chosen because of experiments showing that higher concentrations of acid did not significantly increase the efficiency of extraction. In ascertaining the relative efficiency and applicability of the two processes, the use of the same menstruum in each case was obviously imperative. For those who believe that higher acidity increases the stability of the finished product, the p_H may be adjusted to the desired level by the direct addition of the acid to the mixed percolates. This particular point requires much clarification, and will be dealt with later by a presentation of experimental evidence on the influence of p_H upon stability of the fluidextract. A brief discussion of the practical aspects of the adjustment of p_H is, however, necessitated by a recent publication by Wokes and Elphick (11) in which reference was made to an earlier communication by the present writer (12). This discussion follows Table III.

The results in Table III show conclusively that Fluidextracts of Ergot prepared by Type Process "C" are invariably superior from the standpoint of potency to those prepared by the present official process. A slight difference in p_H in the products yielded by the two processes is probably caused by a loss of hydrochloric acid during the concentration of the exhaust percolate involved in Type Process "B."

TABLE III.—TYPE PROCESS "B" COMPARED AS TO POTENCY AND p_H WITH TYPE PROCESS "C," FOR THE MANUFACTURE OF FLUIDEXTRACT OF ERGOT. 100-GM. PORTIONS OF DRUG USED IN ALL CASES. VOLUME OF EACH FINISHED FLUIDEXTRACT WAS 100 CC.

Drug.	Alkaloid Content of Finished F. E. Prepared by. Type Process "B." Mg./Cc.	p_H.	Type Process "C." Mg./Cc.	p_H.	Potency Gained through Use of Type Process "C." Mg./Cc.
7	0.27	4.67	0.37	4.54	0.10
8	0.46	5.18	0.61	4.97	0.15
9	1.00	5.36	1.44	5.17	0.44
10	0.93	4.88	1.27	4.55	0.34
11	0.75	4.87	0.98	4.66	0.23
12	0.57	5.31	0.71	5.12	0.14

In terms of Ergotoxine Ethanesulphonate.

In addition to such results obtained on a laboratory scale, the writer has been privileged to introduce Type Process "C" and observe similar comparisons in the preparation of Fluidextract of Ergot on a commercial manufacturing scale. Assays were run on the crude ergot involved in each case; the "reserve" and "exhaust" percolates and finished product of Type Process "B" were tested, and in the case of Type Process "C," all three percolates as well as the finished product were assayed. In these observations, the greater efficiency of Type Process "C" was clearly evident in every case. Experience thus gained has brought out several points of particular interest to pharmaceutical manufacturers with reference to Type Process "C." In applying this process on either laboratory or commercial scale production, these studies have shown that the proportions of activity contained, respectively, in the three percolates are subject to considerable variation. Such variations appear to be due, *first*, to a natural difference in ease of extraction of different lots of ergot; *second*, to differences in construction details of extraction equipment; and *third*, to personal equation of the operator particularly with respect to the rate of percolation. Such variations are, however, of little importance in practice, since the final product consisting of the mixed percolates will necessarily contain the total activity extracted. All observations show Type Process "C" to be from 20 to 40% more efficient than Type Process "B" for the manufacture of Fluidextract of Ergot.

In manufacturing Fluidextract of Ergot by this process, it is highly advantageous to know accurately the potency of the lot of drug involved. Only with such knowledge can one avoid the danger of obtaining a product sub-standard as to potency. Attempts at concentration result in a loss of activity which is unnecessary under proper control. In adjusting the potency of the finished product, reduction of potency should never be accomplished by the simple addition of menstruum. The potency should be reduced in such cases by continued percolation until the mixed percolates show the required potency, or until exhaustion is complete as indicated by the tests given above. In the event the potency becomes lowered to the required level before exhaustion is complete, the finished product may be set aside, and the additional weak percolate obtained from exhausting the drug may be stored in the cold room and used as the first menstruum for the next lot to be manufactured.

Type process "C" may also be used to advantage when assaying crude ergot by the official Cock's Comb method. In this case, percolation must be continued until exhaustion is complete as proven by the above tests even though the total volume becomes greater than 1:1. Rarely is it necessary to appreciably exceed this volume to ensure exhaustion, and never does the volume become so great as to interfere with the accuracy of the Cock's Comb method.

STABILITY OF FLUIDEXTRACTS PREPARED BY TYPE PROCESS "C."

Since proposing the change from Type Process "B" to Type Process "C," the question of comparative stability of the finished products has frequently been raised. Studies upon stability have been in progress for over two years, but are not yet ready for reporting in detail. It is possible to state at this time, however,

that, other conditions being identical, Type Process "C" Fluidextracts have proved to be fully as stable as Type Process "B" Fluidextracts.

ADJUSTMENT OF p_H OF FLUIDEXTRACT OF ERGOT.

Following the well-known work of Swanson (8) dealing with the influence of p_H upon the stability of Fluidextract of Ergot, considerable attention has been directed toward this factor by several workers. Swanson's results indicated that the optimum p_H for stability was in the region of p_H 3.0. The writer (12), in 1930, made recommendations relating to this factor, but even at the present time the subject needs clarification both as to the desirability of adjusting the p_H and also as to the method of accomplishment. In 1930, Wokes and Elphick (11) reported observations on extraction and p_H as related to the ergot problem, and stated that

> "Marvin R. Thompson (8)—has recently published a series of recommendations regarding ergot, which will probably exert an important influence on the ergot monographs in the next edition of the U. S. Pharmacopœia. On the basis of Swanson's results, he suggests that, in order to ensure efficient extraction of ergot, and maximum stability of the product, the amount of hydrochloric acid used should be very carefully controlled, both during the process of extraction and in the finished product. Apparently, he assumes that control of the amount of hydrochloric acid used will be sufficient to ensure a fixed p_H."

They then very adequately prove this "assumption" to be incorrect. It is important to point out that the writer in making the recommendation thus referred to by Wokes and Elphick, was very fully aware of the fact that the use of a controlled amount of acid in the manufacture of Fluidextract of Ergot would not ensure a fixed p_H in the finished product. A private communication prompted them to very kindly publish a withdrawal of their criticism (14). The recommendation in question was deliberately so worded after careful consideration of all available evidence relating to p_H and stability. The writer believed then as now, that while a fairly acid p_H possibly favors the stability of solutions or extracts containing ergot alkaloids under certain conditions of storage, there is even to the present time no sufficient evidence which would warrant the time and effort necessary to accurately adjust the p_H at a certain fixed level. Smith and Stollman (3) obtained results which indicated that decreasing the p_H of Fluidextracts of Ergot by varying it between 5.2 and 2.2 does not favor its stability. At approximately the same time, Swanson and co-workers (13) reported further studies on this problem, from which they concluded that ". . . no definite conclusions can be formulated that a certain hydrogen-ion concentration prevents the deterioration of the fluidextract or a solution of the pure ergot alkaloid," although their results caused them to state that their study would be pursued further. Thus it should be clearly apparent that the use of a carefully controlled amount of acid in the extraction menstruum can be made to ensure that the p_H of the finished product will fall, for example, between 3.0 and 5.0 in spite of the great and likewise variable buffer capacity of the usual run of ergot, provided that the extraction equipment is constructed of proper material. Existing evidence, including our own, does not at present indicate that there is any advantage in attempting to attain a level below p_H 4.0. Indeed a series of fluidextracts adjusted at p_H 4.5 to 5.5 have been observed during one year to retain their potency fully as well as those containing

more acid. The details of this study will appear later, since no conclusions of value can be drawn at present.

The above quoted statement recommending control of acidity of the finished fluidextract as well as of the menstruum was made because of knowledge then at hand that certain manufacturers of this product were using extraction equipment constructed of materials which reacted with the acid with the result that all of the acid used in the menstruum did not appear in the finished product. Proper p_H determinations can be utilized to detect such a condition, this condition being objectionable not only because of the loss of acid, but also because of the appearance of foreign soluble matter in the finished product.

Since Wokes and Elphick (11) have published their work on extraction and p_H in detail, and since the observations in our laboratory on this subject completely confirm their results, it is felt that there would be little justification in taking the space necessary for presenting our detailed observations. The study on this phase of the ergot problem is now sufficiently complete to warrant certain statements of fact which should prove helpful, particularly with respect to the adjustment of p_H as follows:

1. Ergot is comparatively rich in substances capable of exerting a buffer effect, particularly phosphates, although the phosphates do not account for the total buffer capacity. Other inorganic as well as organic substances contribute to this effect. Obviously, therefore, any extract of ergot cannot show the same p_H value as the menstruum used.

2. The buffer capacity varies considerably from sample to sample. Therefore, even though menstrua of identical p_H are used, fluidextracts from different lots of ergot are subject to considerable variation as to p_H. There is no way to ensure a definite fixed p_H in a finished fluidextract by simply using a menstruum of a determined fixed p_H.

3. Having determined the p_H of a given fluidextract, the amount of acid necessary to raise the acidity to a certain desired p_H value cannot be calculated without first accurately determining the buffer capacity of the sample. It consumes much less time and effort to make the adjustment by simply adding the acid in small portions until the desired p_H level is attained.

4. Ergot is distinctly acid in reaction and highly buffered. Whether the diluted alcohol menstruum is acidified, alkalinized or neutral, the first extract issuing from the percolator is acid in reaction, showing a value in the vicinity of p_H 5.0 to p_H 6.0. As percolation proceeds and the buffer substances become extracted, the p_H of the issuing percolate gradually approaches that of the original menstruum employed, not attaining the value of the original menstruum, however, until extraction is complete.

For example, when a neutral menstruum is used, the first percolate shows an acidity in the region of p_H 5.3. As extraction progresses the p_H value gradually rises toward neutrality, ultimately reaching the p_H of the menstruum (in the region of p_H 7.0).

If an acidified menstruum is used, showing, for example, a value of p_H 2.0, the first percolate will show an acidity in the region of 5.3 as in the case of the neutral menstruum. Then as percolation proceeds, the p_H value of the issuing percolate gradually becomes lowered toward the p_H value of the original menstruum (2.0).

When an alkalinized menstruum is used, showing, for example, a value of p_H 9.0, the first percolate will again show an acidity in the region of p_H 5.0 to 6.0. Then as percolation proceeds, the p_H value of the issuing percolate gradually becomes raised toward the alkaline p_H value of the original menstruum.

From the above comments regarding p_H, it is obvious that the use of either a neutral or an acidified menstruum for the preparation of Fluidextracts of Ergot will result in products showing an acid p_H value. Owing to the buffer capacity of ergot, which varies considerably from lot to lot, the p_H of the finished fluid-

extract will necessarily show a lower acidity than that shown by the acidified menstruum employed, and the actual p_H of different lots of finished product is subject to considerable variation even though a menstruum of fixed p_H is employed.

The author is greatly indebted to Mr. C. T. Ichniowski and Miss Dorothy Schmalzer for making a great many p_H determinations, and to Dr. E. G. Vanden Bosche for his very active interest in supervising this phase of the work.

NOTE: The studies dealing with isolation and pharmacologic action of the various constituents and preparations of ergot, particularly with respect to the recent clinical observations of Moir and Dale (15), will be reported shortly in a suitable publication.

SUMMARY AND CONCLUSIONS.

I. Certain factors influencing the extraction of ergot have been studied and discussed.

II. A detailed description of a satisfactory technique for applying the Isolated Rabbit Uterus method of Broom and Clark has been presented.

III. The official U. S. P. X process for the manufacture of Fluidextract of Ergot has been critically studied as to efficiency. Experimental results have been presented showing that this process does not provide for the appearance of the total activity of the drug in the finished fluidextract, thereby providing for gross inaccuracies in the official method of assay for crude ergot, and likewise providing for economic loss in the commercial manufacture of this product.

IV. A method of extraction, which avoids the error in assaying crude ergot resulting from the inefficiency of the official extraction process, has been described. The only objection to this method lies in the fact that the extracted activity is contained in a concentration too low to permit of the use of the official Cock's Comb method. The percolate must be tested by the more sensitive Isolated Rabbit Uterus method or the Colorimetric method.

V. Chemical tests for proving exhaustion of the drug of activity have been developed and described, and their limitations indicated.

VI. The U. S. P. General Type Process "C" for fluidextracts, has been studied upon ergot. This process was found to be very significantly superior, from the standpoint of efficiency, to the Type Process "B" now specified by the U. S. P. A change from Type Process "B" to Type Process "C" was recommended to the U. S. P. Committee of Revision in November 1931, on the basis of these results, *first*, because Type Process "C" afforded more accurate results in the assay of crude ergot, and *second*, because this process avoids a considerable loss of activity in actual manufacture of the product. This product, of course, is suitable for direct assay by either the official Cock's Comb, the Rabbit Uterus or the Colorimetric method. In utilizing this process for assaying crude or powdered ergot, the chemical tests for exhaustion should be employed.

VII. The p_H factor in extracting ergot has been discussed.

REFERENCES.

(1) Thompson, JOUR. A. PH. A., 18 (1929), 1106.
(2) Wokes and Elphick, *Quart. J. Pharm. and Pharmacol.*, 2 (1929), No. 4, 539.
(3) Smith and Stollman, *J. Pharmacol. and Exp. Ther.*, 18 (1931), 621.
(4) Smith, *Public Health Report* No. 26; Vol. 45 (1930), 1466.

(5) Broom and Clark, *J. Pharmacol. and Exp. Ther.*, 22 (1923), 59.
(6) Burn and Ellis, *Pharm. J.*, 118 (1927), 384.
(7) Pattee and Nelson, *J. Pharmacol. and Exp. Ther.*, 36 (1929), 85.
(8) Swanson, JOUR. A. PH. A., 18 (1929), 1127.
(9) Thompson, *Ibid.*, 19 (1930), 113.
(10) Thompson, *Ibid.*, 19 (1930), 718.
(11) Wokes and Elphick, *Quart. J. Pharm. and Pharmacol.*, 3, No. 4 (1930), 599–625.
(12) Thompson, JOUR. A. PH. A., 19 (1930), 705.
(13) Swanson, Powell, Stevens and Stuart, *Ibid.*, 21 (1932), 320.
(14) Wokes and Elphick, *Quart. J. Pharm. and Pharmacol.*, 4, No. 1 (1931), 101.
(15) Moir and Dale, *Brit. Med. J.* (June 18, 1932), 1119.

PHARMACOPŒIAL EXHIBIT AT THE A. M. A. CONVENTION.

Herewith is shown the United States Pharmacopœial exhibit, installed at the convention of the American Medical Association, Milwaukee, during the week of June 12th. The exhibit was arranged by courtesy of the College of Pharmacy of the University of Wisconsin, and Edward J. Ireland and Al Rheineck were responsible for the display.

U. S. P. Exhibit at Milwaukee A. M. A. Meeting.

On the left of the picture may be seen an illustrated history of the Military Pharmacopœia of 1778, known as the Lititz Pharmacopœia. In the picture is shown Dr. William A. Brown, military surgeon with George Washington's army during their stay at Lititz, Pennsylvania; the Moravian Brethren's house in which the Pharmacopœia was written; to the left of Dr. Brown's photograph is a copy of the early pharmacopœia. The pharmaceutical preparations in the foreground were made by the pharmacy students according to the original formulas.

Continuing from the left may be seen pictures of modern pharmacopœias, then a reproduction of the Ebers Papyrus, an Epitome of Claudius Galen written in 1571, a copy of Dioscorides'

Materia Medica, two volumes of Hippocrates Medical Works, six early medical writings from German and Italian cities; pharmacopœias from Italy, France, India, Germany, England, Ireland, Scotland, Japan. A complete set of the United States Pharmacopœia features the center of the exhibit; in the immediate center, there were living plants of *Lobelia syphilitics*. Along the right wall may be seen a display of Dover's Powder with its pharmacopœial history. The old wooden mortar was one obtained from Syria, and is reputed to be over three hundred years old. Photographs on the walls show prominent pharmacopœial workers; note also July JOURNAL A. PH. A., page 591.

THE NATIONAL FORMULARY EXHIBIT AT THE AMERICAN MEDICAL ASSOCIATION CONVENTION.

For the third successive year, the National Formulary occupied a booth in the Scientific Exhibit at the Convention of the American Medical Association, held this year at Milwaukee, during the week of June 12th.

Much that has been said concerning the previous N. F. exhibits (see JOUR. A. PH. A., August 1931, page 742, and June 1932, page 536) might be repeated here, for the physicians in attendance showed the same enthusiasm regarding the items shown, and the idea in general, as was indicated both in the Philadelphia and the New Orleans displays.

It will be recalled that at the Philadelphia meeting two years ago the exhibit consisted entirely of vehicles, and it is doubtful whether the N. F. can ever present anything of more general interest than this group of preparations so useful in prescription writing. At the New Orleans convention several of these more valuable vehicles were again shown together with an additional group of popular N. F. items. Again the vehicles received the greatest attention. Consequently

National Formulary Exhibit.

when it came time to determine what was to be included in the 1933 presentation, it was decided to again repeat some of these vehicles. So far as the physicians in attendance are concerned, this plan does not mean repetition, for one finds that the great majority of visitors are from local or nearby territory, this, in fact, being particularly true when meetings are held in such diversified sections of the country. The correctness of this statement was borne out by the fact that the vehicle section of the exhibit once more received the greatest attention.

The general lay-out followed that of past exhibits, and the overhead cards were the same as those used last year to such good effect. The center or rear section displayed the following ve-

hicles: Syrup of Cinnamon, Aromatic Syrup of Eriodictyon, Syrup of Glycyrrhiza, Syrup of Raspberry, Compound Elixir of Taraxacum, Compound Elixir of Vanillin.

In each case actual prescriptions were prepared showing the particular masking ability of the vehicle in question and physicians were quite delighted in tasting many of these prescriptions, to find that the mask was nearly perfect. The Syrup of Cinnamon was again used for Salicylates, the Glycyrrhiza and Raspberry for Bromides or salty preparations, while the Eriodictyon was shown with Quinine, attention being called to the recent work of Fantus which explains the value of this product with bitter alkaloids. The Compound Elixir of Taraxacum was again shown with Phenobarbital, a combination giving a compound prescription which has its advantages in cases of this type.

On the left side were again exhibited solid petroxolin and Compound Menthol Nebula together with Solution of Aluminum Acetate and Zinc Paste, all of which received considerable attention. The right side was taken up with Aromatic Castor Oil, Emulsion of Castor Oil, Emulsion of Cod Liver Oil and Egg and Solution of Iron Peptonate.

It is rather difficult to imagine it, but the Aromatic Castor Oil received as much attention as the best vehicle. Few physicians as well as few pharmacists realize how thoroughly the disagreeable oily taste of Castor Oil is covered in this product. The aromatics not only completely cover the taste but also seem to destroy the heavy oily feeling so characteristic of the plain oil. One physician, an obstetrician, declared that becoming acquainted with this one preparation made attendance at the convention worth while. A number of physicians noted the Latin title and were quite pleased when they realized they could prescribe this old "stand-by" in Latin, as that, together with the masked taste, would never give it away as "Castor Oil."

In the Cod Liver Oil Emulsion particular attention was called to the use of Tincture of Sweet Orange Peel as a preservative and flavor. This replaced the alcohol in the regular formula while simple syrup was used in place of syrup of tolu, no additional flavoring agent being required. The result is splendid, the orange taste remaining long after the Cod Liver Oil taste has disappeared. This revised formula will probably be accepted for the new N. F.

Nearly a thousand booklets were distributed during the Convention and the demands for samples of prescriptions were so numerous that it was necessary to obtain an additional supply of the paper spoons used for sampling.

It is unfortunate that more pharmacists do not realize the great desire on the part of physicians for information such as was given here. There is no question in the mind of the writer that one of the greatest opportunities for development of professional work and a spirit of confidence in the pharmacist, lies in just such a program as the N. F. has barely touched in these presentations. The physicians realize their need of this information and are more than anxious to obtain it. Why should pharmacists neglect such an opportunity to serve?—ADLEY B. NICHOLS.

PLANT SCIENCE SEMINAR.

The following letter has been mailed to members of the Plant Science Seminar:

The Seminar will hold its annual meeting at Madison, Wisconsin, August 21st to August 25th. Headquarters will be at 115 Langdon Street, the Chi Omega Sorority House. Arrangements for rooms have been made as follows: One dollar each for the first night and fifty cents for each following night. The rooms may be retained for the Seminar and A. PH. A. Convention if desired. The House is conveniently located near the lake and not far from the Headquarters Hotel of the A. PH. A. Convention. The rooms are excellently furnished with twin beds A few large rooms have three beds which will be reserved for parties of three. The entire house will be at our disposal and the large rooms on the first floor will be available for our meetings. The house maintains a private pier in the lake and the committee suggests that you bring your bathing suits.

It is very important that we have your reservation as soon as possible in order that we may make final arrangements. Please send your reservation to F. J. Bacon, Sunset Drive, Shorewood Hills, Madison, Wisconsin.

We are enclosing a program and maps of Madison and the scheduled collecting trip. Bring your hiking clothes and collecting equipment.

Please bring the enclosed circular to the meeting with you, since no further program will be printed.

BIBLIOGRAPHY OF PHARMACEUTICAL RESEARCH

Compiled by A. G. DuMez, Reporter on the Progress of Pharmacy.

All articles in these lists will be presented in abstract form in the bound volumes of the Year Book, which is issued annually. Those desiring abstracts immediately can obtain them for a fee of one dollar each by communicating with A. G. DuMez, University of Maryland, School of Pharmacy, N. W. cor. Lombard and Greene Sts., Baltimore, Maryland.

APPARATUS AND MANIPULATIONS.

Wruble, Milton
Studies in percolation
JOUR. A. PH. A., 22 (1933), 641

PHARMACOPŒIAS AND FORMULARIES.

Anon.
Review of the new Danish Pharmacopœia
Pharm. J., 131 (1933), 31
Stainier, Carl
Some remarks on the Belgian Pharmacopœia IV
J. pharm. Belg., 15 (1933), 441, 459

PHARMACEUTICAL PREPARATIONS.

Azzolini, B.
Liquid extract of equisetum
Officina, 5 (1932), 80; through *Chem. Abstr.*, 27 (1933), 3289
Eschenbrenner, H.
Sterilization of sodium bicarbonate solution
Pharm. Zentralh., 74 (1933), 396
Gore, L. F.
Tincture of hyoscyamus
Pharm. J., 130 (1933), 483
Hersant, E. F., and Linnell, W. H.
Stability of ergot preparations
Pharm. J., 131 (1933), 3
Jorek, E.
New ointment bases
Pharm. Ztg., 78 (1933), 667
Lum, E. A.
Arsenical solution, B. P., 1932
Pharm. J., 130 (1933), 412
Neuman, Alfred
Spirit of ethyl nitrite
Pharm. Ztg., 78 (1933), 682
Obergard, I. A.
Preparation of Burow's solution
Khin. Farm. Prom. (1933), 19–22; through *Chem. Abstr.*, 27 (1933), 3289
Pajetta, E.
Changes and keeping qualities of ferrous iodide syrups
Officina, 5 (1932), 261; through *J. Soc. Chem. Ind.*, 52 (1933), 523
Regnier, Jean, *et al.*
Loss in anesthetic power of cocaine solutions under the influence of heat and prolonged storage
Bull. sci. pharmacol., 40 (1933), 353
Tonn, O.
Use of yeast preparations in the making of pills
Pharm. Zentralh., 74 (1933), 377

PHARMACOLOGY, TOXICOLOGY AND THERAPEUTICS.

Barbour, Henry G., and Fisk, Merl E.
Liver damage in dogs and rats after repeated oral administration of cinchophen, tolysin and sodium salicylate
J. Pharmacol. & Exper. Therap., 48 (1933), 341
Chen, K. K., *et al.*
Pharmacological action of peimine and peiminine
JOUR. A. PH. A., 22 (1933), 638
Christensen, B. V., and Lynch, H. J.
Effect of anthelmintics on the host. I. Tetrachlorethylene. II. Hexylresorcinol
J. Pharmacol. & Exper. Therap., 48 (1933), 311
Cutting, W. C., *et al.*
Action and uses of dinitro-phenol
J. A. M. A., 101 (1933), 193
Defandorf, James H.
Studies on the bioassay of digitalis: Frog methods
JOUR. A. PH. A., 22 (1933), 599
Fouts, P. J., and Zerfas, L. G.
Liver-gastric tissue preparations in treatment of pernicious anemia
J. A. M. A., 101 (1933), 188
Geiger, J. C.
Methylene blue solutions in potassium cyanide poisoning
J. A. M. A., 101 (1933), 269
Gersdorff, W. A.
Comparison of the toxicity of nicotine and anabasine
J. Am. Chem. Soc., 55 (1933), 2941

Gutman, Alexander B., *et al.*
Comparison of effect of diiodotyrosine and inorganic iodine in hyperthyroidism
J. A. M. A., 101 (1933), 256
Magidson, O. J., and Strukow, I. Th.
Derivatives of 8-aminoquinoline as antimalarial preparations
Arch. Pharm., 271 (1933), 359
Offerhaus, C., and Baert, C. G.
Anesthetics, particularly cocaine and novocaine
Pharm. Weekbl., 70 (1933), 617, 655
Rappaport, B. Z., and Reed., C. I.
Effect of viosterol of high potency in hay fever and related conditions
J. A. M. A., 101 (1933), 105
Rath, Erich, and Schunck, C.
Hypnotic properties of cyclopentenyl-ethylbarbituric acid
Münch. med. Wochenschr., 80 (1933), 564; through *Chem. Abstr.*, 27 (1933), 3288
Regnier, M. T., and Simonnet, H.
Contribution to the biologic assay of the parathyroid hormone
J. pharm. chim., 17 (1933), 560
Roe, Harold E.
Fatal case of methemoglobinemia following the administration of bismuth subnitrate
J. A. M. A., 101 (933), 352
Schlenk, W., *et al.*
Synthetic experiments in the series of sterols and sexual hormones
J. Soc. Chem. Ind., 52 (1933), 209T
Wells, C. Alex.
Reaction after the injection of sodium morrhuate
Brit. Med. J. (1933), 674

BOTANY AND PHARMACOGNOSY.

Ajello, T.
Investigations on the active principle in Attractylis gummifera
Gazz. chim. ital., 63 (1933), 99; through *Chem. Abstr.*, 27 (1933), 3556
Dieterle, H., and Kaiser, Ph.
Constituents of the rhizome of Curcuma domestica
Arch. Pharm., 271 (1933), 337
Fuji, K., and Shimada, H.
Constituents of the root of Sanguisorba officinalis L.
J. Pharm. Soc. Japan, No. 616 (1933), 120
Hayden, Alice H., and Jordan, C. B.
Chemical study of Ma Huang
Jour. A. Ph. A., 22 (1933), 616
Henrotin, Marie
Contribution to the study of Strophanthus seed
J. pharm. Belg., 15 (1933), 479
Jaretzky, R., and Kühne, F.
Pharmacognosy of Tanacetum vulgare
Arch. Pharm., 271 (1933), 353
Kofler, L., and Marek, M.
Sarsaparilla in the new German Pharmacopœia
Pharm. Monatsh., 14 (1933), 127
Martin-Sans, E., and Mathou, Thérése
Falsified angustura
Bull. sci. pharmacol., 40 (1933), 350

ALKALOIDS AND GLUCOSIDES.

Biedebach, Felix
Note on the Helch reaction for pilocarpine
Apoth.-Ztg., 48 (1933), 723
Craig, L. C.
New synthesis of nornicotine and nicotine
J. Am. Chem. Soc., 55 (1933), 2854
Heldt, L. J., and Forbes, G. S.
Absorption and fluorescence spectra of the acid sulphates of quinine and ten derivatives in aqueous sulphuric acid solution
J. Am. Chem. Soc., 55 (1933), 2701
Jermstad, Axel, and Östby, Ottar
Iodometric determination of caffeine
Dansk Tids. Farm., 7 (1933), 117
Kofler, L., and Kofler, A.
Melting point and crystal forms of morphine
Arch. Pharm., 271 (1933), 387
Mohs, Paul
Glucosides of Digitalis lanata
Arch. Pharm., 271 (1933), 393
Orechoff, A.
Alkaloids of Berberis heteropoda
Arch. Pharm., 271 (1933), 323
Sabatucci, Nicoletta
Detection of quinotoxine in some cinchona barks and in galenical preparations
Scienza farm., 1 (1933), 4; through *Chem. Abstr.*, 27 (1933), 3556
Stoll, A., and Kreis, W.
Digitalis glucosides
Bull. sci. pharmacol., 40 (1933), 321

OILS, FATS AND WAXES.

Fiero, George W.
Chemical examination of the oil of ergot
Jour. A. Ph. A., 22 (1933), 608
Royce, H. D.
Stability of fats and oils
Ind. Eng. Chem., Analyt. Edit., 5 (1933), 244

ESSENTIAL OILS.

Anon.
Aniseed, fennel and star-anise oil
Parf. France, 11 (1933), 106; through *Pharm. J.*, 131 (1933), 37

Dafert, O., and Capesius, V.
Oil of Chenopodium ambrosioides
Pharm. Presse, Wissensch. Heft., 38 (1933), 69

Louveau, G.
Aging and altering of essential oils
Rev. marq. parfum. savon (1932), Nos. 1–6; through *Chem. Abstr.*, 27 (1933), 3556

Reed, R. M.
Identification of phenols in essential oils
Perf. & Ess. Oil Rec., 24 (1933), 190

Vignoli, L.
Estimation of crystallizable apiol
Bull. sci. pharmacol., 40 (1933), 344

ANALYTICAL METHODS AND RESULTS.

Benedetti-Pichler, A. A., and Schneider, Frank
Quantitative isolation of ether from dilute solutions
Ind. Eng. Chem., Analyt. Edit., 5 (1933), 255

Collins, W. D., *et al.*
Recommended specifications for analytical reagent chemicals
Ind. Eng. Chem., Analyt. Edit., 5 (1933), 288

Fischer, G. G.
Colorimetric investigation of the saffron test
Apoth.-Ztg., 48 (1933), 747

Guerbet, André
Remarks on the estimation of iodine by the Carius method
J. pharm. chim., 17 (1933), 556

Gutman, A. B., *et al.*
Assay of thyroid by chemical estimation of the thyroxine content
Proc. Soc. Exptl. Biol. Med., 29 (1932), 1198; through *Chem. Abstr.*, 27 (1933), 3555

Haines, R. T. M.
Variation in samples of sodium morrhuate
Lancet (1933), 5, 719, 748

Jenkins, Glenn L., and Hoshall, Edward M.
Assay of N. F. preparations containing pepsin
Jour. A. Ph. A., 22 (1933), 625

Munro, A. C., and Seifert, R.
Estimation of pepsin
Pharm. J., 130 (1933), 432

Noto, F., and Perciabosco, F.
New method for the identification of oxalic acid in citric acid
Ann. chim. applicata, 23 (1933), 21; through *Chem. Abstr.*, 27 (1933), 3287

Palmer, W. W., and Leland, J. P.
Observations on Mörch's method for the standardization of thyroid preparations
Proc. Soc. Exptl. Biol. Med., 29 (1932), 1195; through *Chem. Abstr.*, 27 (1933), 3555

Raquet, D., and Pinte, P.
Rapid iodometric estimation of phosphites and hypophosphites individually or in mixtures
J. pharm. chim., 18 (1933), 5

Rohmann, C.
Contribution to the quantitative analysis of aluminum acetate solution
Pharm. Zentralh., 74 (1933), 393

Vishnesvska, K.
Determination of phenolphthalein in tablets
Farm. Zhur. (1933), 77

Weissmann, G.
Determination of phenacetin, aspirin and antifebrin
Z. anal. Chem., 93 (1933), 31; through *Chem. Abstr.*, 27 (1933), 3557

INORGANIC CHEMICALS.

Goris, A., and Richard, F.
Zinc peroxides of commerce
Bull. sci. pharmacol., 40 (1933), 336

ORGANIC CHEMICALS.

Florence, G.
Acetophenone and some of its derivatives
Bull. sci. pharmacol., 40 (1933), 325

Gardner, J. H., *et al.*
Anesthetics containing the morpholine ring. II
J. Am. Chem. Soc., 55 (1933), 2999

Gulati, K. Ch., *et al.*
Antiseptics and anthelmintics. I. 1-Alkyl-2-naphthol
J. prakt. Chem., 137 (1933), 47; through *Chem. Abstr.*, 27 (1933), 3558

Hinegardner, W. S.
Racemization of chaulmoogric and hydnocarpic acids
J. Am. Chem. Soc., 55 (1933), 2831

Leger, E.
Hydrolysis of the aloins
J. pharm. chim., 18 (1933), 25

Milshtein, A., and Rozenberg, G.
Preparation of ether for anesthesia
Farm. Zhur. (1933), 77

Rising, M. M., *et al.*
Synthesis of colored derivatives of phenobarbital
J. Am. Chem. Soc., 55 (1933), 2817

Wagner, Jauregg, Th.
Chemistry of the vitamines
Arch. Pharm., 271 (1933), 369

A STUDY OF VEHICLES FOR MEDICINES.

BY BERNARD FANTUS, H. A. DYNIEWICZ AND J. M. DYNIEWICZ.

(*Continued from page 658, July 1933.*)

ISO-ALCOHOLIC ELIXIRS.

It is now thirteen years (4) since the idea of "iso-alcoholic elixir" was brought forward. By this term is meant an elixir of an alcoholic strength just sufficient to dissolve the medicament for which the elixir is to serve as a vehicle. To accomplish this, we require two basic elixirs: 1, an *aqueous elixir* containing a minimal percentage of alcohol and an *alcoholic elixir* containing a high percentage of alcohol. These two have to be mixable in all possible proportions. The advantage of using the term "iso-alcoholic elixir" (5) in prescribing, lies in the fact that it is practically impossible for the physician to remember the exact alcoholic strength required for dissolving all the various drugs he prescribes. It would surely be a great comfort to him, could he, by employing this designation, feel assured that the pharmacist would always deliver a perfectly clear and compatible preparation. This the pharmacist could readily do, possibly with the aid of his reference books, if he had the two basic elixirs in stock. What happens when aromatic elixir is used instead of iso-alcoholic elixir is shown by the following experiments:

EXPERIMENTS.

1. Tincture of digitalis 0.5 cc. mixed with enough aromatic elixir to make a teaspoonful gives a copious precipitate. The same dose added to a mixture of alcoholic elixir 3 parts, aqueous elixir 1 part—the proportions of alcohol and water used in the menstruum—is, of course, perfectly clear.

2. Tincture of veratrum viride, 0.5 cc. added to aromatic elixir 4 cc., precipitates even more copiously than does the digitalis mixture. Using the alcoholic elixir, which is required by the strongly alcoholic menstruum employed in the extraction of the drug, yields a perfectly clear and safe preparation.

3. Tincture of aconite 0.3 cc. whose menstruum is alcohol 7 parts, water 3 parts, precipitates with the official aromatic elixir 4 cc.; but naturally does not, when added to iso-alcoholic elixir made in the proportions of alcoholic elixir 7, and aqueous elixir 3.

4. Tincture nux vomica 0.5 cc. plus aromatic elixir 4 cc. is cloudy. The same dose added to the proper mixture of alcoholic and aqueous elixirs, 3 to 1, remains clear.

5. Tincture colchicum seed, 2 cc., added to aromatic elixir, throws down a few flocculi. Using alcoholic elixir 3, and aqueous elixir 2, gives a clear preparation.

6. Tincture lobelia, 1 cc. added to a mixture of equal parts of aqueous and alcoholic elixirs remains clear, while a precipitate forms with the aromatic elixir.

7. Fluidextract of buchu, 2 cc. added to aromatic elixir yields a copious precipitate, while a clear solution results when the dose is added to the alcoholic elixir.

8. The same is true when a dose of 0.1 cc. of fluidextract of cannabis indica is added to aromatic elixir, while the alcoholic elixir yields a clear solution.

In all these experiments, the average pharmacopœial dose was added to enough elixir to make a teaspoonful. The turbidity resulting in all of these cases with the aromatic elixir of the U. S. P. is not only unsightly but introduces, in some of these instances, an element of danger, as many of these precipitates are toxic. Insufficient shaking of the bottle before taking would lead to a possibly dangerous inequality of dosage. In those preparations, on the other hand, in which the iso-alcoholic elixir was used, a perfectly clear preparation results.

In case of chemicals, the term iso-alcoholic elixir would obviously mean that mixture of aqueous or alcoholic elixir, or either of them alone, that would give a clear solution with the minimal percentage of alcohol.

Thus, for instance, a physician who might want to prescribe the average Pharmacopœial dose of sodium bromide (1 Gm.) in elixir; and who doubted, as he should, that this quantity would dissolve in aromatic elixir, might prescribe it with iso-alcoholic elixir as the vehicle. The pharmacist, knowing that this salt dissolves much more readily in water than in alcohol, would employ the aqueous elixir for its solution. The U. S. P. aromatic elixir does not dissolve more than 0.60 Gm. (10 gr.) of sodium bromide per teaspoonful.

The use of the term "iso-alcoholic elixir" by the prescriber and the proper interpretation of it, by the pharmacist, would avoid the interesting incompatibility arising, when the physician prescribes chloral and bromide dissolved in elixir. In the aqueous elixir it is perfectly compatible. The same doses dissolved in the official elixir, results in the "salting out" of chloral alcoholate. If the attempt is made to dissolve the chloral and bromide in the alcoholic elixir, a great excess of sodium bromide remains undissolved.

A physician who might desire to prescribe an average official dose of terpin hydrate (0.25 Gm.) in solution, need not worry about its solubility, if he specifies iso-alcoholic elixir as the solvent. The pharmacist would dissolve this dose in the alcoholic elixir, and thus secure a perfect solution of an active dose of terpin hydrate. Parenthetically, be it remarked, that the dose of the terpin hydrate in the N. F. elixir of terpin hydrate is merely 0.087 Gm., approximately $1^1/_2$ grains, which is a rather small dose.

Professor Langenhan, having found that the two elixirs for the preparation of iso-alcoholic elixir, as previously elaborated, produced a turbidity in those dilutions in which the aqueous elixir strongly predominated (under certain temperature conditions), it was found desirable to increase the alcoholic strength of the "aqueous" elixir, to approximately 10 per cent of alcohol. This increase in the alcoholic strength might also improve its keeping qualities, which ought to be excellent in view of the fact that the preparation is now quite saturated with sugar. Our revised formula, therefore, would be as follows:

ELIXIR AQUOSUM.

Aqueous Elixir.

Elix. Aqu.

Compound Spirit of Orange	**10.0 cc.**
Alcohol	**100.0 cc.**
Glycerin	**200.0 cc.**
Sucrose	**320.0 cc.**
Distilled Water, a sufficient quantity,	
To make	**1000.0 cc.**

Mix the alcohol, glycerin and water, and add to them the compound spirit of orange, agitating thoroughly from time to time, and permit to stand twenty-four hours. Filter through a hard filter (Whatman 50) returning, if necessary, the first portions of the filtrate until it passes through clear. Dissolve the sucrose in the filtrate by agitation or percolation, and add enough of the solvent mixture to make the product measure 1000 cc.

ELIXIR ALCOHOLICUM.

Alcoholic Elixir.

Elix. Alc.

Compound Spirit of Orange	**4.0 cc.**
Gluside	**3.0 Gm.**
Glycerin	**200.0 cc.**
Alcohol, a sufficient quantity,	
To make	**1000.0 cc.**

Dissolve the compound spirit of orange and the gluside in the alcohol, add the glycerin and sufficient alcohol to make the product measure 1000 cc. and filter.

ELIXIR ISO-ALCOHOLICUM.

Iso-Alcoholic Elixir.

Elix. Iso-Alc.

Aqueous Elixir	**a certain proportion**
Alcoholic Elixir	**a certain proportion**

Mix them.

Iso-alcoholic elixir is intended to serve as a general vehicle for various medicaments that require solvents of different alcoholic strengths. When, therefore, iso-alcoholic elixir is specified in a prescription, that proportion of its two ingredients is to be used that will produce a perfect solution.

For liquid galenicals, the strength of iso-alcoholic elixir to be used is the same as that of the menstruum or solvent employed in the preparation of the galenical.

When galenicals of different alcoholic strengths are used in the same prescription, the iso-alcoholic elixir to be used is to be of such strength as to secure the best solution possible under the circumstances. This will generally be found to be the average of the alcoholic strength of the several ingredients.

For non-extractive substances, the lowest alcoholic strength of iso-alcoholic elixir should be chosen that will yield a perfect solution. For substances that are readily soluble in water and less soluble in alcohol, the aqueous elixir is to be used. For substances that are readily soluble in alcohol and insoluble in water, the alcoholic elixir is to be employed.

TABLE FOR ADJUSTMENT OF ALCOHOLIC STRENGTH OF ISO-ALCOHOLIC ELIXIR.

Aqueous Elixir.	Alcoholic Elixir.	Suitable as Vehicle for Preparations Requiring the Following Alcoholic Strengths:
Aqueous Elixir		0–10%
4 parts	1 part	10–20%
3 parts	1 part	20–30%
2 parts	1 part	30–40%
1 part	1 part	40–50%
1 part	2 parts	50–60%
1 part	3 parts	60–70%
1 part	4 parts	70–80%
Alcoholic Elixir		80–95%

A comparison of the two above given formulas will show the apparent incongruity that there is a great deal more of the compound spirit of orange in the aqueous than in the alcoholic elixir. This may seem all wrong, in view of the fact that much more of the compound spirit of orange will dissolve in the alcoholic

than in the aqueous elixir. In point of fact, however, it is not necessary to add more than the 0.4% of the compound spirit of orange as suggested in the formula for the alcoholic elixir, to make it fully as strongly flavored as the aromatic elixir which no doubt contains, when cleared of the excess of oil, even a smaller percentage than that. The only justification for using so large a proportion of the compound spirit of orange in the preparation of the aqueous elixir lies in the observation we made that this larger proportion produces a more fully flavored elixir than any smaller proportion would. It seemed as well flavored as if we had used the more water-soluble "terpeneless" oil of orange. As the expense of this latter quality of the oil of orange is prohibitively great, we believe that we are dissolving out some of this portion from the large excess of the oil of orange we are using; and it is cheaper to waste the rest than to insist upon the terpeneless oil.

Incidentally, it might be noted that the alcoholic elixir, as it contains no sugar, might be used as a pleasant vehicle for medicaments intended for the diabetic, in whom the sugar-containing aromatic elixir would be contraindicated.

CONCLUSIONS.

1. The present formula for the preparation of aromatic elixir is very time-consuming.

2. To lessen the time required, the following modifications of the official formula are proposed: (*a*) lessen the viscosity by dissolving the sugar after clarification; (*b*) dispense with the necessity of using talcum by securing dispersion of the oil mixture in droplets large enough to be intercepted by a hard filter; (*c*) by permitting the mixture to stand for some time with occasional agitation before filtration, saturation of the solvent can, no doubt, be secured even by the larger droplets. A formula embodying these principles is submitted.

3. Formulas are advanced for an "aqueous elixir" and an "alcoholic elixir," which are mixable with each other in all proportions. The official recognition of these elixirs would make it possible for the physician to prescribe "iso-alcoholic elixir," meaning by the term an elixir of the *same* alcoholic strength as the menstruum of the galenic preparation for which it is to serve as vehicle.

REFERENCES.

(1) Silver, *Practical Druggist*, 48 (1930), 37.
(2) Schifflet, *Ibid.*, 48 (1930), 17.
(3) Krantz and Carr, "Further Studies in Filtration," JOUR. A. PH. A., 21 (1931), 785.
(4) B. Fantus, *Ibid.*, 9 (1920), 708.
(5) B. Fantus and C. M. Snow, *Ibid.*, 10 (1921), 277.

IVY POISONING.

The Ohio State Division of Conservation is advocating the use of a 5 per cent solution of potassium permanganate as a first aid or emergency treatment for ivy poisoning, in response to many inquiries from anglers and campers. It should be applied by swabbing with cotton or soft cloth. This treatment is recommended by Dr. J. F. Couch of the U. S. Department of Agriculture.

The Division also broadcasts the information that ivy poisoning can be prevented in many cases by using the following wash, devised by Dr. J. B. McNair of Field Museum, Chicago: 5 per cent solution of ferric chloride in a 50-50 mixture of water and glycerin. Before going out, wash the exposed part of the skin and allow the solution to dry before subjecting the exposed parts to possibility of infection. The iron in the mixture combines with the poisonous element in the ivy and changes it into a harmless, non-poisonous compound.

DETERMINATION OF THE REASONABLE OR PERMISSIBLE MARGIN OF ERROR IN DISPENSING.*

BY MARVIN J. ANDREWS.[1]

INTRODUCTION.

The compounding and dispensing of medicines ordered by physicians is the primary function of the pharmacist in his relationship to the public. The education and training which the pharmacist is required to have before he is granted a license to practice and the legal restrictions otherwise thrown about the practice of pharmacy are indicative of the importance which the public attaches to the proper exercise of this function. It is believed that the great majority of pharmacists of this country recognize fully the responsibility which is theirs in this regard and take every precaution that can reasonably be expected of them to compound prescriptions accurately. In spite of the precautions taken, however, errors in compounding and dispensing are made. Occasionally, they are of such magnitude that untoward symptoms of unmistakable origin develop after the medicine is administered, when the error is detected and brought to notice. More frequently, however, the error made is comparatively small or the reaction of the patient is attributed to the malady instead of the remedy and it passes by unnoticed.

To err when reasonable precautions are taken to avoid doing so cannot be attributed to ignorance, carelessness or negligence. It must be attributed to other factors—factors over which even the most careful compounder has little or no control. The personal equation, for instance, enters into every operation involved in the filling of a prescription. In addition, there are the variations in the calibration of measuring utensils and the inaccurate adjustment of scales or balances to be reckoned with. As a matter of fact, it is impossible to fill any prescription without deviating to some extent from the quantities ordered by the prescriber. No measurement or weighing is ever free from error due to one or more of the factors mentioned above; but with the exercise of care, such error can be reduced to a reasonable minimum. To determine the magnitude of this reasonable minimum is the purpose of the studies reported in this series of papers.

Some work has already been done along this line. It is possible that fairly extensive investigations have been made in some of the countries of Continental Europe in which dispensing is carried on under close governmental supervision; but in Great Britain and in this country, where this rigid control is lacking, studies sufficiently extensive and comprehensive to justify the use of the data obtained as a basis for fixing the limit of reasonable or permissible error in the compounding of all but a few of the many types of prescriptions filled in the pharmacies of to-day do not appear to have been made. A résumé of the work of this character done in the two countries last named over the past sixty years follows.

As far back as 1872, C. William Grassley[2] examined 165 samples of Seidlitz powders purchased in this country and in Canada for accuracy with respect to ingredient content.

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* Section on Practical Pharmacy and Dispensing, A. PH. A., Toronto meeting, 1932.

[1] In collaboration with A. G. DuMez, Professor of Pharmacy, School of Pharmacy, University of Maryland.

[2] PROC. A. PH. A., 20 (1872), 273–300.

Only 2 of the 165 were found to have been accurately prepared. The error in the 163 other samples was attributed largely to the fact that the powders were made by measuring instead of weighing. Depending on the pressure exerted in filling, the capacity of the larger cavity (used for measuring the Seidlitz mixture) of the double-cup measure in general use was found to be 95 to 120 grains and that of the smaller cavity (used for measuring the tartaric acid) 20 to 24 grains.

In an editorial which appeared in the *Pharmaceutical Journal and Pharmacist* for April 12, 1924,[1] mention is made of some dispensing tests carried out in London in 1886. Those who made these tests are reported to have stated that only 6% of the prescriptions compounded by "chemists and druggists" were found to be inaccurate, and to have expressed the view that 10% was an allowable margin of error in individual cases. Unfortunately these are all of the details carried in the editorial and the original report printed in *Chamber's Journal* is not available.

In 1889, E. B. Stuart and E. B. Tainter[2] published a report on the degree of accuracy attained by 37 pharmacists in dispensing the following prescriptions for powders: Prescription No. 1, ferric oxide, 0.1 Gm., sugar 10 Gm., to be divided into 10 powders. Prescription No. 2, Dover's powder, 3.0 Gm., to be divided into 6 powders. Prescription No. 3, powdered rhubarb, magnesia, of each 2.5 Gm., to be divided into 15 powders.

The average error was found to be 4.8% for prescription No. 1, 9.4% for prescription No. 2 and 9.45% for prescription No. 3. For prescription No. 1, the error was less than 5% in 21 instances, between 5% and 10% in 14 instances, between 10% and 15% in one instance and more than 20% in 1 instance. For prescription No. 2, the error was less than 5% in 22 instances, between 5% and 10% in 9 instances, between 10% and 15% in 5 instances and 16.5% in 1 instance. For prescription No. 3, the error was less than 5% in 17 instances, between 5% and 10% in 5 instances, between 10% and 15% in 8 instances and more than 20% in 6 instances.

The *Pharmaceutical Journal and Pharmacist* for December 9, 1922[3] calls attention to some of the results of an investigation made by the Public Health Committee of the Middlesex County Council to ascertain the accuracy with which medicinal powders were dispensed. In one case, the 6 powders supplied weighed from $2^3/_4$ to 5 grains each, averaging 4 grains. In two other instances, the 6 powders supplied varied in weight from 5 to 7 grains each. In two cases, no powder weighed more than $5^1/_2$ grains. A subsequent examination of the scales and weights of the pharmacists concerned is reported to have revealed that the inaccuracies were not wholly due to maladjustment of the weighing appliances.

Within the past year and a half, two papers dealing with the subject have appeared in print, one by John Butler[4] reporting the results of an investigation made in England and the other by Dr. John C. Krantz, Jr.,[5] reporting the results of the examination of certain preparations purchased from pharmacists in Baltimore, Maryland.

In the report made by Mr. Butler, data are given to show the error made by 40 "dispensing chemists" in the compounding of certain liquid potassium bromide mixtures. These data show that in 4 of the 40 potassium bromide mixtures examined, the error with respect to potassium bromide content was greater than 10%; in 34, the error was below 5% and in 27 the error was below 3.5%. Mr. Butler states further that most "chemists" are of the opinion that an error of 10% should be allowed, and that this is accepted by most Pharmaceutical Service Sub-Committees as a fair margin in the dispensing of certain types of mixtures.

Dr. Krantz reported the probable error with respect to potassium iodide content to be 9.55% for 10 samples of Saturated Solution of Potassium Iodide, N. F. V, examined.

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[1] *Pharm. J. & Pharm.*, 112 (1924), 397.

[2] PROC. A. PH. A., 37 (1889), 183–188.

[3] *Pharm. J. & Pharm.*, 109 (1922), 545.

[4] *Ibid.*, 128 (1932), 149.

[5] *Maryland Pharmacist*, 7 (1932), 543–545.

For 17 samples of Tincture of Ferric Chloride, U. S. P. X, examined, the probable error with respect to iron content was computed to be 6.45%. In two batches of twelve 5-grain quinine capsules prepared by pharmacists, the probable error with respect to quinine content was computed to be 25.11% and 5.08%, respectively.

The data presented in the foregoing reports, although inadequate and in some instances unsuited for the purposes of this study, are nevertheless of some value. They at least lend weight to the statement already made, that deviation from the quantities ordered is the general rule in dispensing rather than the exception, and show that there is need for further systematic investigation along these lines to enable us to fix the margin of error which may be accepted as reasonable or permissible. The British appear to have accepted 10% as the "allowable" margin of error for certain types of prescriptions, at least. Whether or not this margin is the proper one for all types of prescriptions still remains to be proven.

EXPERIMENTAL PART.

The different types of prescriptions which the pharmacist is ordinarily called upon to fill may be divided, roughly, into two classes, namely, liquids and solids. With respect to the magnitude and frequency of the error to be expected, the latter class seemed to offer the greatest possibilities because of the more complicated nature of the operations involved in filling prescriptions of that type. For these reasons and because powders and capsules are actually prepared by the pharmacist more frequently than any of the other types of this class, they were selected as the types to be used in beginning this study.

POWDERS.

With respect to the preparation of powders, and this applies to the preparation of capsules as well, the division of the bulk powder into individual doses constitutes the greatest source of error. Furthermore, the error from this source is not constant since the magnitude is dependent to a considerable extent upon the *modus operandi* by which the division is made. Of the many methods which have been suggested for effecting this division, the majority have as their chief aim speed in completing the task rather than accuracy. The following are the methods which are in general use. They were, therefore, used in making the studies reported herein.

(1) The guess by eye method in which small portions of the powder are transferred to papers by means of a spatula; and when all has been thus transferred, the quantities on the different papers equalized as nearly as possible by eye.

(2) The method of blocking and dividing, which consists of transferring the bulk powder to a tile or a piece of glazed paper, building it up into a rectangular pile or a parallelogram, by means of two straight-edged spatulas, and dividing the pile thus formed into the desired number of parts by cutting with a spatula.

(3) The method of weighing, in which the amount to be contained in each powder is weighed off separately. When this method is followed, the last powder will be underweight if the scales have been properly adjusted and the weighings accurately made, because some of the material will adhere to the sides of the mortar in which the powder was mixed or be lost in some other way. This expected deficiency is generally avoided by preparing a sufficient amount of the bulk powder to make one or two extra powders.

In addition to the determination of the frequency and magnitude of error traceable to the *modus operandi* of dividing the bulk powder, the effort was also made to determine to what extent, if any, certain other factors influence the final result. It seemed desirable, for instance, to determine the effect of the nature of the ingredients, the number of ingredients, the size of the individual powders and the number of powders prepared. With these objectives in view, the following prescriptions were filled.

No. 1.

Hydrarg. Chlor. Mit.	gr. ii
Lactos.	gr. iii

M. et ft. chart. No. 1
D. t. d. No. viii
Sig: One powd. every 15 min.

No. 2.

Hydrarg. Chlor. Mit.	gr. $^1/_6$
Pulv. Ipecac.	gr. $^1/_{16}$
Lactos.	gr. i

M. et ft. pulv. No. 1
D. t. d. No. XV
Sig: One every 2 hrs.

No. 3.

Sod. Bicarb.	℥i
Mass. Hydrarg.	℈i

M. et ft. chart. No. viii
Sig: One powd. every 4 hrs. followed by a Seidlitz powder.

No. 4.

Bism. Subnit.	℥i
Phenyl. Salicyl.	℥ss
Carbo. Lig.	℈ii

M. et div. in chart. No. xii
Sig: One t. i. d.

No. 5.

Mag. Oxid.	℥i
Cret. Præp.	℥ii
Pil. Ext. Bellad. Fol.	gr. ii
Ol. Menth. Pip.	gtt. iii

M. et div. in pulv. No. xv
Sig: One powd. $^1/_2$ hr. p. c.

No. 6.

Quin. Sulph.	gr. xv
Pulv. Aloe	gr. x
Ext. Ergot.	gr. ii

M. et ft. pulv. No. xii
Sig: One every 3 hours.

No. 7.

Ext. Casc. Sagr.	gr. i
Ol. Fœnic.	gtt. i
Lactos. *q. s.*	(gr. iv)

M. et ft. chart. No. xii
Sig: One powd. every 4 hrs.

No. 8.

Hydrarg. Chlor. Mit.	gr. ii
Sod. Bicarb.	gr. x

M. et ft. chart. No. vi
Sig: One powd. every 2 hrs.

No. 9.

Mag. Oxid. Pond.	gr. lxxx

Ft. pulv. No. viii
Sig: One powd. in aq. $^1/_2$ hr. p. c.

No. 10.

Pulv. Ext. Bellad.	gr. i
Acetphen.	gr. lx

M. et ft. pulv. No. xii
Sig: One powd. every 4 hrs.

No. 11.

Hydrarg. Chlor. Mit.	gr. i
Bis. Subnit.	gr. xxx

M. et ft. pulv. No. x
Sig: One every hr.

In the actual performance of the tests, the foregoing prescriptions were filled by the members of the senior class in dispensing pharmacy at the School of Pharmacy of the University of Maryland under working conditions very similar to those prevailing in the better type of pharmacies. It is true that these students were inexperienced in comparison with the average practitioner; but it is believed that this lack of experience was offset to a large extent, if not completely, by uniformity in measuring and weighing appliances and the close supervision maintained over each operation by the instructors in charge of the work.

For laboratory practice the class in dispensing is divided into sections of approximately 30 students each, and the work of each section is supervised by 4 instructors. Each prescription was filled by the members of at least one section and in some instances by the members of two sections. The completed powders were checked for accuracy with respect to total quantity by weighing on a fairly sensitive balance. No attempt was made in this series of tests to check the amounts of individual ingredients, except in the case of prescription No. 1.

The results obtained in these tests are given in the tables which follow. In each case, the standard deviation was computed, and such conclusions as have been drawn are based on the use of this quantity of measurement. Other workers, who have reported tests of this character have stated the results in terms of percentage of deviation from the theoretical amount or from the mean. It seemed, however, more to the point to show the closeness with which the individual results are clustered about the mean; and as the quantity used for this purpose in works on general

statistics is the standard deviation (S. D.), it was used in reporting the results of this study. In the derivation of this quantity, the generally accepted formula, S. D. = $\sqrt{\frac{\Sigma d^2}{n}}$ was used, in which Σd^2 represents the sum of the deviations squared, and n the number of observations made.

PRESCRIPTION NO. 1.

Prescription No. 1 was filled by the "guess by eye method" by one section of the class consisting of 30 students as a part of the regular laboratory work. The fact that the results were to be checked for purposes other than routine grading was not made known. These prescriptions were checked for the weight of individual powders. In addition, 10 batches were selected at random from the 30 batches of 8 powders each, and the calomel content of each powder was determined by the assay method given in the U. S. P. X for calomel. The results obtained are given in the Tables I and II.

TABLE I.—PRESCRIPTION NO. 1 (CORRECT WEIGHT OF EACH POWDER = 5 GRAINS).

Batch No.	Weight of Each Powder in Grains. 1.	2.	3.	4.	5.	6.	7.	8.	Total Wt. in Grains.	Av. Wt. in Grains.	S. D.[1]
1	4.500	5.000	5.000	4.500	5.500	5.250	5.500	4.375	39.625	4.953	0.423
2	5.000	5.125	5.125	5.125	5.125	5.250	5.375	4.875	41.000	5.125	0.139
3	4.750	4.625	5.000	5.250	5.250	4.875	5.375	4.500	39.500	4.937	0.286
4	4.875	5.250	4.625	4.875	5.000	5.125	5.625	4.625	40.000	5.000	0.312
5	4.625	5.875	4.875	5.000	5.125	5.625	6.000	4.375	41.500	5.187	0.552
6	5.500	5.250	5.250	5.125	5.250	5.250	5.750	5.000	42.375	5.296	0.215
7	4.625	5.000	5.000	5.000	5.000	5.000	5.125	4.500	39.250	4.906	0.204
8	4.750	4.625	4.875	5.625	4.625	4.625	5.750	4.500	39.375	4.921	0.454
9	4.875	4.375	5.250	4.875	5.375	4.750	5.625	4.375	39.500	4.937	0.423
10	5.000	4.500	4.750	5.000	5.250	5.500	5.500	4.500	40.000	5.000	0.167
11	5.125	4.750	5.000	5.500	5.250	6.000	5.250	4.750	41.625	5.203	0.313
12	4.500	5.250	4.875	5.000	4.250	5.000	6.000	3.875	38.750	4.843	0.608
13	4.875	5.625	6.375	5.250	4.875	5.125	5.625	4.625	41.375	5.171	0.341
14	4.500	4.875	5.125	4.750	5.000	4.500	5.125	4.500	38.275	4.797	0.256
15	4.750	5.250	4.875	4.625	5.250	5.000	6.000	4.125	39.875	4.984	0.513
16	5.500	5.000	5.500	5.000	5.125	5.000	4.500	4.250	39.875	4.984	0.407
17	5.375	5.750	4.750	4.875	4.875	5.000	4.500	4.625	39.750	4.968	0.384
18	5.625	5.000	4.500	5.125	4.625	4.875	5.250	4.875	39.875	4.984	0.333
19	4.875	5.625	5.250	5.125	4.625	4.625	5.625	5.250	41.000	5.125	0.369
20	5.125	5.000	5.000	4.625	5.250	4.750	5.750	4.125	39.625	4.953	0.446
21	4.875	4.875	4.750	4.875	5.000	5.250	5.375	4.750	39.750	4.968	0.214
22	4.875	4.875	4.500	4.875	5.000	5.125	5.375	4.875	39.500	4.937	0.234
23	5.500	4.250	5.250	5.750	4.875	4.750	5.625	4.875	40.875	5.109	0.477
24	5.750	5.625	5.500	5.125	4.500	5.000	4.750	4.750	41.000	5.125	0.428
25	5.125	5.250	4.500	5.500	5.500	5.000	4.500	4.750	40.125	5.015	0.377
26	4.250	4.375	4.625	5.000	5.250	5.375	4.750	5.125	38.750	4.843	0.384
27	5.000	5.125	4.875	4.500	4.750	4.625	5.250	4.875	39.000	4.875	0.233
28	5.000	5.000	5.125	4.750	5.250	4.875	5.125	4.875	40.000	5.000	0.153
29	5.000	5.125	4.500	4.500	4.625	4.750	5.625	4.875	39.000	4.875	0.353
30	4.875	5.125	4.625	4.875	5.500	4.750	5.125	4.250	39.125	4.890	0.350

[1] Av. S. D. = 0.345, which is equivalent to an average deviation from the theoretical of 6.90%.

It will be observed that in the case of the weight of individual powders, the average standard deviation is 0.345 gr., or 6.91% of the prescribed amount. Fourteen of the 30 batches filled fall within the average S. D. of 0.345 gr., while the remaining 16 fall within twice the average S. D., or 0.691 gr.

TABLE II.—PRESCRIPTION NO. 1 (CORRECT PERCENTAGE OF CALOMEL = 40).

Batch No.	Per Cent of Calomel in Each Powder. 1.	2.	3.	4.	5.	6.	7.	8.	Average Per Cent.	S. D.[1]
1	40.96	35.14	36.36	41.99	41.64	38.05	40.87	39.29	39.29	2.37
2	40.55	46.89	37.06	37.28	39.89	41.56	41.09	40.45	40.59	2.84
3	40.25	40.15	40.05	39.75	39.50	40.30	39.82	40.25	40.01	0.27
4	39.85	39.90	40.12	39.89	40.27	40.15	40.27	39.80	40.03	0.19
5	37.46	37.38	39.60	39.05	37.60	37.83	34.80	40.66	38.05	1.65
6	37.66	42.04	41.32	41.59	39.42	39.67	40.27	39.99	40.24	1.32
7	42.09	40.34	39.79	41.66	40.16	40.16	41.18	41.39	40.85	0.78
8	36.93	36.27	36.24	37.90	36.73	35.67	35.60	34.21	36.19	1.02
9	40.20	40.50	39.32	38.83	39.34	38.43	41.64	32.74	38.87	2.50
10	33.91	39.53	43.07	40.82	39.07	40.15	38.53	38.13	39.15	2.45

[1] Av. S. D. = 1.54, which is equivalent to an average deviation from the theoretical of 3.84%.

In the case of the calomel content, the average standard deviation amounts to 1.54, or 3.84%, based on a calculated content of 40 per cent. Five of the batches assayed for calomel content fall within the average S. D., while the remaining 5 fall within twice the average S. D., or within 7.68% of the correct amount.

On further examination of Table II, it will be observed that the standard deviation for the calomel content in the individual batches of powders is as low as 0.19 and as high as 2.84.

The error in the case of calomel content was probably due in greater part to insufficient trituration in the mixing of the ingredients, or failure to scrape all of the material from the pestle and sides of the mortar. Factors, other than these, affecting the results are errors in weighing, loss during transfer and triturating the calomel in a porous mortar before adding the lactose.

PRESCRIPTIONS NOS. 2–11.

Prescriptions Nos. 2 to 11 were studied with a view to determining to what extent all of the factors heretofore mentioned contribute to the total error. The prescriptions filled in this series of tests were selected with the primary objective in view of determining to what extent, if any, the following contribute to the total error: number of ingredients, nature of the ingredients, number of powders to be made and the amount of material in each powder. To secure data to show to what extent the method used in dividing the bulk powder is responsible for the total error; in some of these prescriptions the bulk powder was divided by the "guess by eye method," in others by the blocking and dividing method and in still others by weighing off quantity for each powder.

The finished prescriptions were checked for accuracy of weight of the individual powders only, and the standard deviation was computed from the results obtained. Before these prescriptions were given out for filling, the students were instructed with respect to the method to be used in dividing the powders, and they were told that their work would be checked for accuracy.

TABLE III.—STANDARD DEVIATION OF PRESCRIPTIONS NOS. 2–7.

Batch No.	Prescriptions. No. 2.	No. 3.	No. 4.	No. 5.	No. 6.	No. 7.
1	0.172	0.797	0.305	1.336	0.172	0.371
2	0.241	1.115	0.903	1.425	0.518	0.056
3	0.237	0.605	0.111	0.584	0.260	0.261
4	0.177	0.533	0.226	0.648	0.442	0.310
5	0.158	1.048	0.673	1.342	0.503	0.138
6	0.119	0.162	0.740	0.284	0.500	0.046
7	0.290	0.292	0.711	0.223	0.310	0.116
8	0.219	0.152	0.951	0.218	0.601	0.086
9	0.154	0.140	0.121	0.287	0.228	0.069
10	0.228	0.846	0.579	1.251	0.189	0.063
11	0.128	0.270	0.985	0.861	0.241	0.072
12	0.360	0.697	0.508	1.113	0.165	0.048

13	0.205	0.729	0.217	0.945	0.692	0.067
14	0.169	0.336	0.473	0.351	0.300	0.132
15	0.114	0.863	0.818	1.007	0.241	0.241
16	0.233	0.211	0.072	0.911	0.697	0.180
17	0.140	0.135	0.069	0.226	0.052	0.310
18	0.268	0.460	0.436	0.585	0.036	0.179
19	0.222	0.582	1.180	0.548	0.136	0.275
20	0.115	0.345	1.131	0.530	0.580	0.103
21	0.169	1.025	0.521	0.118	0.276	0.279
22	0.191	0.162	1.043	1.138	0.104	0.276
23	0.069	0.200	0.551	1.190	0.026	0.081
24	0.133	0.787	0.450	0.187	0.513	0.241
25	0.238	0.653	0.830	1.120	0.117	0.210
26	0.128	0.496	0.147	1.027	0.071	0.181
27	0.121	0.330	0.895	0.234	0.117	0.184
28	0.113	1.096	0.582	0.154	0.083	0.352
29	0.191	0.515	0.531	0.374	0.345	0.363
30	0.248	0.168	0.464	0.652	0.314	0.276
Av. S. D. =	0.185	0.525	0.574	0.696	0.294	0.186
Av. % =	18.10	5.25	5.30	5.72	13.06	3.72

TABLE IV.—STANDARD DEVIATION OF PRESCRIPTIONS NOS. 8–11.

Batch No.	Prescriptions. No. 8.	No. 9.	No. 10.	No. 11.	Batch No.	Prescriptions. No. 8.	No. 9.	No. 10.	No. 11.
1	0.246	0.041	0.571	0.267	31	0.392	0.391	0.448	0.120
2	0.473	0.454	0.258	0.224	32	0.213	0.496	0.902	0.365
3	0.261	0.165	0.560	0.229	33	0.212	0.206	0.965	0.107
4	0.238	0.066	0.295	0.256	34	0.116	0.458	0.985	0.150
5	0.239	0.082	0.949	0.327	35	0.257	0.019	0.253	0.373
6	0.327	1.200	0.643	0.097	36	0.062	1.035	0.072	0.129
7	0.294	0.647	0.772	0.335	37	0.171	0.108	0.177	0.150
8	0.471	0.630	0.672	0.074	38	0.133	0.454	0.660	0.075
9	0.042	1.074	0.604	0.245	39	0.232	0.366	0.219	0.150
10	0.363	0.901	0.815	0.333	40	0.276	0.302	0.794	0.075
11	0.132	0.049	0.362	0.322	41	0.089	0.605	0.100	0.150
12	0.432	0.763	0.240	0.069	42	0.387	1.058	0.578	0.172
13	0.221	1.158	0.421	0.377	43	0.314	0.286	0.502	0.064
14	0.133	0.037	0.111	0.365	44	0.205	0.940	0.657	0.150
15	0.208	1.172	0.645	0.225	45	0.198	0.898	0.412	0.149
16	0.232	0.520	0.332	0.154	46	0.057	0.557	0.252	0.074
17	0.152	0.209	0.941	0.150	47	0.243	0.319	0.389	0.075
18	0.392	0.176	0.797	0.261	48	0.199	0.608	0.903	0.110
19	0.162	0.435	0.587	0.160	49	0.365	0.735	0.860	0.112
20	0.151	0.206	0.061	0.075	50	0.267	0.829	0.931	0.078
21	0.450	0.521	0.885	0.098	51	0.085	0.658	0.371	0.168
22	0.335	0.529	0.821	0.075	52	0.126	0.744	0.689	0.098
23	0.306	0.056	0.454	0.152	53	0.191	1.081	0.911	0.178
24	0.352	0.309	0.485	0.100	54	0.086	0.504	0.166	0.331
25	0.204	0.829	0.356	0.182	55	0.156	0.528	0.326	0.180
26	0.161	0.250	0.829	0.077	56	0.046	0.629	0.430	0.337
27	0.186	0.829	0.560	0.331	57	0.112	0.187	0.560	0.224
28	0.221	1.175	0.036	0.140	58	0.046	0.155	0.615	0.375
29	0.227	1.178	0.281	0.093	59	0.260	0.082	0.212	0.267
30	0.450	0.156	0.243	0.044	60	0.151	0.330	0.644	0.367
					Av. S. D. =	0.228	0.523	0.526	0.185
					Av. % =	11.40	5.23	5.26	5.97

As already stated, the greatest source of error is the division of the bulk powder into individual doses. It may be said further with respect to the methods of filling that the error will be least in those cases in which the powders are divided by weighing. This is shown to be true by the results obtained for prescription No. 7, in which the average standard deviation is only 0.186, 17 of a total of 30 batches falling within the average S. D., while the remaining 13 fall within twice the average S. D.; and in prescription No. 11, in which the average standard deviation is 0.185, 38 of the total of 60 batches falling within the average S. D., 20 within twice the average S. D. and the remaining 2 within three times the average S. D.

When the blocking and dividing method is used, a slight increase in the average standard deviation results. This is revealed by the results obtained for prescription No. 8, in which the average standard deviation is 0.228, 35 of a total of 60 batches falling within the average S. D., 23 within twice the average S. D., and the remaining 2 within three times the average S. D.; and in prescription No. 6, the average standard deviation of which is 0.294, 17 of a total of 30 batches falling within the average S. D., 10 within twice the average S. D. and 3 within three times the average S. D.

The "guess by eye method" is the least accurate of the methods studied. The results obtained by this method of division are shown in the case of prescription No. 1, in which the average S. D. is 0.345, only 14 of a total of 30 batches falling within the average S. D., and the remaining 16 falling within twice the average S. D.; or in prescription No. 9, in which the average S. D. is 0.523, 33 of a total of 60 batches falling within the average S. D., 19 within twice the average S. D. and 8 within three times the average S. D.

On examination of the results given for prescriptions Nos. 9, 3, 4 and 5, it will be observed that the number of ingredients contained in the powder mixture has a slight effect upon the standard deviation. By increasing the number of ingredients, the number of operations of weighing and transferring are increased, which in turn results in an increase in the standard deviation. When there is only one ingredient, as in prescription No. 9, the average S. D. is 0.523; with two ingredients, as in prescription No. 3 the average S. D. is 0.525; with three ingredients, as in prescription No. 4, the average S. D. is 0.574; and with four ingredients, as in prescription No. 5, the average S. D. is 0.696.

The nature of the ingredients also plays a part in increasing or decreasing the standard deviation in divided powder prescriptions as shown in prescriptions Nos. 1, 5, 10, 6 and 7. The standard deviation for the simple admixture of powders is lower than when the prescription contains a pillular extract or volatile oil in addition to the dry powder. This is to be expected as it is more difficult to weigh a sticky mass, such as a pillular extract, and completely transfer and incorporate it with other material than if it were a dry powder.

The number of powders dispensed also influences the final result. This is shown in the case of prescriptions Nos. 8, 1, 10 and 5, which call for 6, 8, 12 and 15 powders, respectively. The average standard deviation in these instances is 0.228, 0.345, 0.526 and 0.696, which shows that the magnitude of the error increases directly with the number of powders made.

The amount contained in each powder has a decided effect on the standard deviation, as well as on the percentage deviation from the theoretical amount, which is shown in the following table.

TABLE V.—EFFECT OF SIZE OF INDIVIDUAL POWDER ON STANDARD DEVIATION.

Prescription Number.	Theoretical Weight of Each Powder in Grains.	Average Standard Deviation.	Percentage Deviation from the Theoretical.
2	1	0.185	18.10
8	2	0.228	11.40
1	5	0.345	6.90
3	10	0.525	5.25
5	12	0.696	5.72

The foregoing data show that the standard deviation increases directly with the weight of the individual powders whereas the percentage deviation from the theoretical amount shows a corresponding decrease. This is to be expected, as a deviation of $^1/_4$ grain in a powder weighing 1 grain results in a 25 per cent error, while a deviation of a $^1/_4$ grain in a powder weighing 10 grains

results in an error of only $2^1/_2$ per cent. The results show further that there is a marked decrease in the error with an increase in weight up to 5 grains, where it remains fairly constant. Incidentally, the practical significance of this is that powders divided by the methods other than weighing should be made to weigh a minimum of 5 grains.

The results of the foregoing tests are summarized in Table VI, which follows. This table shows, in addition to the actual number of batches of powders falling within the standard deviation and multiples thereof, the percentage of the totals which these constitute. It also shows the grand totals falling within these limits.

(*To be continued*)

ASH LIMIT OF DRUGS.

L. W. Winkler (*Pharm. Zentralh.*, 73 (1932), 593, 612, 705). The drug was first freed from adhering earthy matter, then powdered and passed through a sieve of 5-mm. mesh. It was then transferred to a large mortar and stirred for some minutes without pressure from the pestle, in order to assist in removal of impurities. This was continued until no foreign particles were distinguishable under a lens. The powder was then dried for one or two days over quicklime.

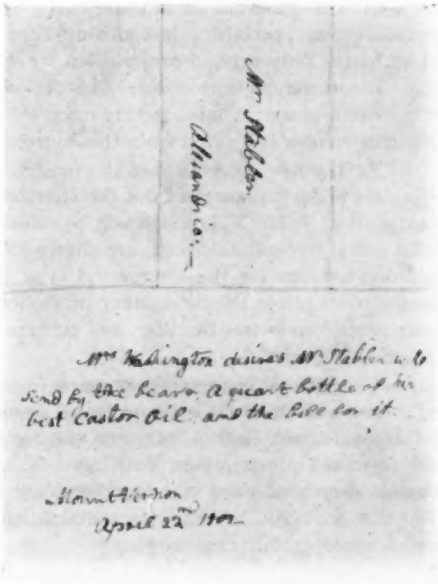
About 1 Gm. of pure sand was placed in a quartz crucible of 5 cc. capacity and 10 drops of fuming nitric acid were added. After evaporation of the acid, the crucible was heated for five minutes, then cooled on a thick metal plate and weighed when cold. About 0.5 Gm. of the powdered prepared drug was added and the drug and sand thoroughly mixed by means of an iron nail. The crucible and contents were weighed, gently heated until the drug was carbonized, and then heated more strongly for five minutes. After cooling, the contents were again carefully mixed with the iron nail in order to break up any large particles of carbonaceous matter, and the crucible again strongly heated. After cooling, the contents were again mixed and then 10 drops of fuming nitric acid were added. The acid was evaporated and the crucible heated to redness, cooled and weighed.

In order to ensure complete decomposition of organic matter a further treatment with nitric acid is advocated. The use of powdered oxalic acid as described in the German Pharmacopœia is not recommended since oxalic acid on combustion always gives rise to some carbon.

Figures for about 100 drugs are given, in most cases for both the whole and the powdered drug, obtained from two or three different sources.

The ash limits of the German Pharmacopœia seem to be too high, it is suggested that both an upper and a lower limit should be set in future editions, and a table of proposed limits is given. In order to evaluate an unground drug, the ash of both the crude drug and the sieved powder should be determined, the difference indicating the amount of earthy matter. The ash of powdered drugs of good quality is not in general greater than that of the cleaned whole drug.

The author suggests that drug houses should always insert the ash limit after the name of the drug, in order to distinguish their goods from inferior grades.—Through *Quarterly Journal of Pharmacy*.


Mrs Washington desires Mr Stabler will send by the bearer a quart bottle of his best Castor Oil and the Bill for it.

Mount Vernon April 22nd 1797

Reproduction from original order to Stabler's Pharmacy, Alexandria, Va.—Martha Washington.

THE PROFESSIONAL PHARMACY.*

BY FRANK A. DELGADO AND ARTHUR A. KIMBALL, U. S. DEPARTMENT OF COMMERCE.

(*Continued from page 693.*)

CHAPTER III. PRESCRIPTION PRICE TRENDS.

AVERAGE PRICE OF PRESCRIPTIONS BY TYPE OF PRESCRIPTION IN PROFESSIONAL AND COMMERCIAL TYPE DRUG STORES—CHANGING PRICE TRENDS IN 1910, 1920 AND 1930.

Prescription prices in the professional stores in 1930 were somewhat lower than in the commercial stores, in every type of prescription except nonnarcotic specialties. The fact that the professional stores filled a larger proportion of prescriptions calling for manufacturers' specialties than the commercial type stores, as shown later in Table XXVIII, and had to keep a wider variety of specialties in stock, is the probable explanation of the higher price for specialty prescriptions.

The showing that average prescription prices were lower in the professional stores will come as a surprise to some readers. It might be thought that professional store prescription prices would be higher than those in commercial type stores for several reasons. For example, the salaries paid the pharmacists or prescription clerks are often higher in professional stores, more prescription equipment is often required and more extensive delivery service is given. But if a pharmacist in a professional store fills five times as many prescriptions each day as one in a commercial type store, the salary cost per prescription in the professional store would be less in spite of the fact that the salary paid per man was higher. Of course, the fact that the pharmacist in the commercial type store also attends to duties in other departments, so that his full salary would not be charged to prescriptions, should be considered. But it probably will be found that the salary cost per prescription is lower in the professional drug store than in the commercial type store. Information concerning operating cost and net profit in the various types of drug stores is now being compiled. When that information is available, the reason for high or low prices will probably be explained.

There is probably a much faster turnover of "staple" prescription items in the professional store, and this would result in lower cost. A possible exception to the fast turnover assumption, manufacturers' specialties, has already been pointed out above, specialties being shown in Table XI to be the only type of prescription for which the professional stores charged higher prices than the commercial type stores. It is probable that in professional stores prescriptions are priced on a more systematic basis, paying more attention to elements of cost, due to the fact that their principal volume is derived from this source.

At any rate, regardless of the reason, the two professional stores studied did charge lower prices for prescriptions than did the commercial type drug stores. This finding is further substantiated in Table XII, which will be discussed later. The prices charged for prescriptions by three other professional stores are shown in that table, and in only one case were they higher than the average for the commercial type stores. However, Stores A and B were inclined to charge lower prices than the other professional stores. Store A has been in business for many years, since long before the War, and perhaps it thus has the inherited and prejudicial tradition of low pre-war prices.

The increase in prescription prices from 1910 to 1920, and from 1920 to 1930 is very interesting. The price increase is found for all types of prescriptions, being considerable in every case. The increase from 1910 to 1920 was much greater than that from 1920 to 1930, the latter, in the case of mixed prescriptions, both narcotic and nonnarcotic, being very small. The only case where a decreased price was found was with official narcotic prescriptions, which were lower in 1930 than in 1920. Perhaps an examination of wholesale prices of narcotic chemicals over this period would explain this showing.

According to figures obtained from the Bureau of Labor Statistics, United States Department of Labor, the value or purchasing power of the dollar in 1910 was $1.31, and in 1920 only

* See Table of Contents, page 671, July issue of the JOURNAL. This installment covers Chapters III and IV, which see.

$0.58, if we consider the 1930 dollar to be worth exactly $1.00. It is interesting to compare the increase in prescription prices over the 20-year period with the fluctuation in the value of the dollar during the same period. The higher purchasing power of the dollar in 1910 is an explanation of the lower average prices in that year. However, the 1930 dollar is worth close to twice as much as the 1920, but during that period, prescription prices increased, but at a much smaller rate than in the preceding 10 years.

In both commercial type and professional drug stores, official prescriptions had the lowest average price and specialties the highest, considerably higher than for official prescriptions. Mixed prescriptions were priced about half-way between official and special prescriptions.

Of the questionnaire stores, 64.7 per cent have a schedule of prescription prices and 71.8 per cent charge less for prescriptions containing only official ingredients. The proprietors in 80 per cent of the cases reported that they have been able to maintain prescription prices during the depression.

Due to the low average price of prescriptions in 1910, $0.51 each, it would have taken 1686 prescriptions in 1910 to bring in the same dollar volume that would be brought in by 1000 prescriptions in 1930 at the average price of $0.86 that year. However, it must be remembered that in 1910, physicians were in the habit of writing more prescriptions. Also, there were fewer drug stores per capita and the cost of operating a pharmacy was less. Therefore, it is probably safe to say that in 1910 prescription business was at least as lucrative as it is to-day.

TABLE XI.—AVERAGE PRICE OF PRESCRIPTIONS BY TYPE OF PRESCRIPTION IN PROFESSIONAL AND COMMERCIAL TYPE DRUG STORES—PRICES FOR 1910, 1920 AND 1930 IN A PROFESSIONAL DRUG STORE.

Type of Prescription.	Average Price of Prescriptions. Prescriptions from Professional Stores.[1] 1930.	1920.	1910.	Prescriptions from Commercial Type Stores.[2] 1930.
Narcotics:				
Official	$0.81	$0.84	[3]	$0.96
Mixed	0.91	0.87	[3]	0.98
Specialties	0.91	0.77	[3]	0.96
Total Narcotics	$0.85	$0.84	[3]	$0.97
Nonnarcotics:				
Official	$0.73	$0.66	[3]	$0.84
Mixed	0.85	0.82	[3]	0.93
Specialties	1.04	0.89	[3]	1.02
Total Nonnarcotics	$0.86	$0.76	[3]	$0.91
All Regular Prescriptions:				
Official	$0.75	$0.69	$0.46	$0.86
Mixed	0.86	0.83	0.53	0.93
Specialties	1.03	0.88	0.58	1.02
Total All Prescriptions	$0.86	$0.77	$0.51	$0.92

[1] For the year 1930, these figures are based on the study of 8700 prescriptions from two professional stores; for 1920 and 1910, 1000 prescriptions filled by Store A were analyzed.

[2] These price figures were obtained by the study of 23,963 prescriptions from 13 commercial type drug stores, including two chain store units.

[3] These price figures are not available, for the Federal narcotic law was not operative in 1910, so narcotics and nonnarcotics were not distinguished between nor filed separately.

MONTHLY PRESCRIPTION PRICE TRENDS IN THREE ADDITIONAL PROFESSIONAL PHARMACIES.

The average prescription prices shown in this table were based on the study of a sizable sample of prescriptions for each month of the year in each store. It is interesting to compare these average prices with those shown for two other professional stores in Table XI. While the

average prescription prices in all of these three stores were higher than in the two professional stores reported in Table XI, yet two of these three stores maintained slightly lower prices than the average for commercial type stores, shown in Table XI. Store D, however, priced its prescriptions, both narcotic and nonnarcotic, considerably higher than the other four professional pharmacies, and higher than the average for the commercial type stores. It should be noted that the prescription prices in these three professional pharmacies are based on prescriptions filled during the year 1931, while the prices in Table XI are based on the year 1930, but it is not believed that this fact will make any material difference for purposes of this comparison.

There seems to be no particular trend as to any particular season of the year in which prescription prices were higher. For example, in Store D the average price of narcotic prescriptions is higher during the late fall, winter and early spring months, October through May, while in Store C the price of these prescriptions is highest in the early spring and summer months, March through August. The proprietor of Store C reports that the high average prices of nonnarcotic prescriptions in the summer months were due to a prevalence of gonococcus infections for which certain fairly high-priced proprietary preparations are frequently prescribed. He further states that asthmatic and tubercular patients suffer more in the warm months thus requiring more narcotics, which when prescribed in larger quantities have a higher average price.

The showing for Store E (a St. Louis professional pharmacy mentioned only in this connection) is very unusual, narcotic prescriptions having an average price considerably lower than nonnarcotics. Due to the extra skill and care which must be used, and risk assumed, in filling narcotic prescriptions, it is unusual to find narcotic prescriptions averaging a lower price than nonnarcotics, regardless of the cost of the materials used.

The questionnaire professional stores reported an average price of $1 each for prescriptions, but the average prescription prices ranged among the stores from a low figure of $0.65 to a high average of $2.50.

TABLE XII.—PRESCRIPTION PRICE TRENDS IN THREE PROFESSIONAL PHARMACIES.[1]

Month (1931).	Average Prescription Prices by Type of Prescription. Store C. Narcotic.	Store C. Nonnarcotic.	Store D. Narcotic.	Store D. Nonnarcotic.	Store E. Narcotic.	Store E. Nonnarcotic.
Jan.	$0.84	$0.88	$1.06	$0.98	$0.79	$0.86
Feb.	0.87	0.85	1.02	0.89	0.73	0.87
March	1.00	0.85	1.06	1.00	0.84	0.86
April	1.00	0.84	1.03	0.90	0.75	1.01
May	0.97	0.87	1.14	1.01	0.94	0.90
June	1.20	0.90	0.95	0.97	0.86	0.89
July	1.30	0.94	0.97	1.06	0.85	0.89
Aug.	1.05	0.95	0.91	0.91	0.84	0.93
Sept.	0.97	0.84	0.88	0.93	0.88	1.04
Oct.	0.86	0.92	1.03	0.95	0.88	0.95
Nov.	0.92	0.91	0.92	0.97	0.74	0.99
Dec.	0.93	0.89	1.00	0.98	0.81	0.87
Average	$0.99	$0.89	$1.00	$0.96	$0.82	$0.92

[1] These prescription prices are based on study of from 34 to 37 narcotic prescriptions and from 198 to 253 nonnarcotic prescriptions in each store for each month.

PRICE RANGES OF PRESCRIPTIONS BY TYPE AND NATURE OF PRESCRIPTION.

In making the following analysis, 8700 prescriptions filled by Stores A and B in 1930 were studied. It will be seen that the most popular price range for both narcotic and nonnarcotic prescriptions was from $0.75 to $1.00, inclusive. Slightly more than half of the narcotic prescriptions were priced within this range as compared with 43 per cent of the nonnarcotics. Only 13.5 per cent of the narcotic prescriptions were priced at more than $1.00, as compared with 17.6 per cent of the nonnarcotics. But, on the other hand, there was a smaller proportion of narcotics priced below $0.75, than was true for nonnarcotics.

It seems rather surprising, however, to find that 13.87 per cent of the narcotic prescriptions were priced at less than $0.50, the same being true for only 8.49 per cent of the nonnarcotics. Considering the high cost of narcotic chemicals and drugs and the extra skill and care that must be used and risk that must be taken in filling narcotic prescriptions, it is surprising to find such a large proportion priced at less than $0.50. In the case of 23,963 prescriptions filled by commercial type drug stores, reported on in the first report concerning the prescription department phase of the survey, only 1.31 per cent of the narcotic prescriptions were priced at less than $0.50, while about 26 per cent of the narcotic prescriptions were priced at more than $1.00 by the commercial type stores.

The result of the difference cited above is seen when referring to Table XI, which shows the average price of narcotic prescriptions in Stores A and B to be only $0.85, less than the $0.86 average price of nonnarcotic prescriptions. The average price of narcotic prescriptions in the commercial type drug stores studied was $0.97, as compared with a $0.91 average price for nonnarcotics.

As seen in Table XII, showing the average prescription prices for Stores C, D and E, narcotic prescriptions averaged $0.10 higher than nonnarcotics in Store C, and $0.04 higher in Store D. However, in Store E an unusual condition was found, narcotic prescriptions being priced at $0.82 and nonnarcotics at $0.92.

Table XIII also shows the price ranges for official, mixed and specialty prescriptions, under narcotic, nonnarcotic and total regular prescriptions. It is interesting to note the general uni-

TABLE XIII.—PRICE RANGES OF PRESCRIPTIONS FILLED BY STORES A AND B IN 1930 BY TYPE OF PRESCRIPTION.[1]

Price Range.	Type of Prescription. Official. Number.	Official. Per Cent Total.	Mixed. Number.	Mixed. Per Cent Total	Specialty. Number.	Specialty. Per Cent Total.	All Prescriptions. Number.	All Prescriptions. Per Cent Total.
Narcotic Prescriptions:								
Over $2.00	20	2.06	11	2.11	3	2.78	34	2.12
$1.55–$2.00	28	2.88	20	3.85	7	6.48	55	3.44
$1.05–$1.50	48	4.94	60	11.54	19	17.59	127	7.94
$0.75–$1.00	484	49.79	298	57.31	36	33.33	818	51.13
$0.50–$0.70	212	21.81	107	20.57	25	23.15	344	21.50
$0.25–$0.45	180[2]	18.52	24	4.62	18	16.67	222	13.87
Total	972	100.00	520	100.00	108	100.00	1600	100.00
Nonnarcotic Prescriptions:								
Over $2.00	26	0.87	12	0.64	113	5.08	151	2.13
$1.55–$2.00	49	1.64	28	1.49	85	3.82	162	2.28
$1.05–$1.50	215	7.18	242	12.86	480	21.59	937	13.20
$0.75–$1.00	1267	42.30	968	51.43	819	36.85	3054	43.01
$0.50–$0.70	1098	36.66	553	29.38	542	24.38	2193	30.89
$0.25–$0.45	340[2]	11.35	79	4.20	184	8.28	603	8.49
Total	2995	100.00	1882	100.00	2223	100.00	7100	100.00
All Regular Prescriptions:								
Over $2.00	46	1.16	23	0.96	116	4.98	185	2.13
$1.55–$2.00	77	1.94	48	2.00	92	3.94	217	2.49
$1.05–$1.50	263	6.63	302	12.57	499	21.41	1064	12.23
$0.75–$1.00	1751	44.14	1266	52.70	855	36.68	3872	44.51
$0.50–$0.70	1310	33.02	660	27.48	567	24.32	2537	29.16
$0.25–$0.45	520[2]	13.11	103	4.29	202	8.67	825	9.48
Total	3967	100.00	2402	100.00	2331	100.00	8700	100.00

[1] Refills are not included among the prescriptions studied.

[2] One narcotic and one nonnarcotic official prescriptions were priced under 25 cents.

formity in the price ranges, regardless of the type of prescription. For all types of prescriptions the most popular price was from $0.75 to $1.00, inclusive. Nearly two-thirds of the regular prescriptions priced at more than $2.00 were manufacturers' specialties, specialties also accounting for the largest proportion of the prescriptions priced at from $1.55 to $2.00. On the other hand, nearly two-thirds of the prescriptions priced at less than $0.50 were official prescriptions. The average cost of materials in each specialty prescription was $0.45, as compared with $0.17 for materials in official prescriptions, according to a study of the prescriptions in one store. Considering the cost of specialty ingredients, the fact that they were responsible for a large percentage of the high-priced prescriptions is to be expected. Due to the fact that specialties are responsible for a majority of the items occurring only once each in 10,000 prescriptions, as shown elsewhere in the report, perhaps they should bear an even higher mark-up to cover the cost of maintaining items of infrequent occurrence.

PRESCRIPTION PRICE RANGES COMPARED BETWEEN PROFESSIONAL AND COMMERCIAL TYPE DRUG STORES, AND FOR PRESCRIPTIONS FILLED IN 1910 AND 1920.

The majority of the commercial type drug store prescriptions studied were priced at from $0.75 to $1.00. These prescriptions were filled in 1930. The 8700 professional store prescriptions, also filled in 1930, were priced generally lower than those filled in commercial type drug stores, although nearly half of the professional store prescriptions were also priced at from $0.75 to $1.00. But nearly twice as large a proportion of the professional store prescriptions were priced at less than $0.75 than in the case of the prescriptions from the commercial type drug stores, with a corresponding decrease in the proportion of prescriptions priced at more than $0.75. The only exception to this general trend is found in the high-priced prescriptions, those priced at more than $2.00, of which the proportion was twice as high in the professional store prescriptions, due to the fact that rare expensive remedies are more likely to be requested from a professional pharmacy than a commercial type drug store.

The price ranges for prescriptions filled in 1910 and 1920 show an interesting picture. In 1910, nearly half of the prescriptions were priced at less than $0.50, and 35.5 per cent between $0.50 and $0.75. Only about 2 per cent of the prescriptions studied for 1910 were priced at more than $1.00. It is interesting to compare this with the commercial store prescriptions filled in 1930, where only 2.54 per cent were priced at less than $0.50 and over 21 per cent at more than $1.00. This difference is of course due in large part to the difference in the purchasing power of the dollar in 1910 and 1930, as pointed out previously. Also at that time there were not as many high-priced specialties being prescribed by physicians who confined their prescriptions more to standard official chemicals and galenicals. The prescription prices in 1920 ranged considerably higher than in 1910, but were not as high as in 1930.

TABLE XIV.—PRESCRIPTION PRICE RANGES IN COMMERCIAL TYPE AND PROFESSIONAL DRUG STORES IN 1930, COMPARED WITH PRICE RANGES FOR PRESCRIPTIONS FILLED IN 1910 AND 1920 BY PROFESSIONAL STORE A.

Price Range.	13 Commercial Type Stores.		2 Professional Pharmacies.		Store A (1920).		Store A (1910).	
	Number.	Per Cent of Total.	Number.	Per Cent of Total.	Number.	Per Cent of Total.	Number.	Per Cent of Total.
Over $2.00	248	1.04	185	2.13	21	2.10	5	0.50
$1.55–$2.00	659	2.75	217	2.49	18	1.80	2	0.20
$1.05–$1.50	4,256	17.76	1064	12.23	100	10.00	14	1.40
$0.75–$1.00	13,677	57.08	3872	44.51	351	35.10	139	13.90
$0.50–$0.75	4,513	18.83	2537	29.16	323	32.30	355	35.50
$0.25–$0.45	610[1]	2.54	825[2]	9.48	187[3]	18.70	485[4]	48.50
Total	23,963	100.00	8700	100.00	1000	100.00	1000	100.00

[1] Includes 19 prescriptions priced at less than $0.25.
[2] Includes 2 prescriptions priced at less than $0.25.
[3] Includes 8 prescriptions priced at less than $0.25.
[4] Includes 16 prescriptions priced at less than $0.25.

INCONSISTENCY IN PRESCRIPTION PRICING—PRESCRIPTIONS PRICED BELOW COST.

Throughout the entire study of prescriptions filled in commercial type and professional drug stores, many inconsistencies in prescription pricing were found. In some stores such inconsistencies were less prevalent than in others, but no store was immune. In certain stores the prescriptions were priced in such a haphazard fashion, that the pricing policy might be said to be one of guesswork. Such a policy is undoubtedly a costly and dangerous one to use. For example, in Store 11-B, a prescription containing cocaine alkaloid and liquid petroleum was priced at $0.85, although the materials alone cost $1.45. This did not take into account the cost of the pharmacist's compounding time, or any other cost factors. Such underpriced prescriptions were not a rare occurrence in the stores studied.

Inconsistent pricing also is likely to detract from the good-will which a store has built up. If a customer is charged different prices for the same prescription, or finds that another customer is obtaining the same or a similar prescription for a lower price, it is quite likely to create bad feeling toward the store. Of course, the price charged is usually noted on the prescription, for the pharmacist's guidance in case the prescription is refilled. But if the original price was a matter of guesswork, and did not even cover the cost of materials, every time the prescription was refilled at that price, an additional loss would be incurred.

A few minutes taken after filling the prescription and spent in determining the cost of the ingredients used in compounding it, the cost of the time of the pharmacist who filled it, and the other heavy expenses of the prescription department which must be shared by this prescription, would be time well spent. Thus, the pharmacist would charge a price which would cover all cost elements and allow a reasonable net profit, and which, being determined on a business like basis, would enable the pharmacist to know that his pricing policy was sound, avoiding the possibility of hidden losses and pricing inconsistencies.

One practice which the pharmacist might profitably adopt would be to write the price per ounce on the label of each of his manufacturers' specialty prescription ingredients which are called for most frequently, say the 50 most important specialties. This would take but little time, would save the pharmacist the trouble of looking up the cost of the ingredient at the time he fills a prescription, and would help to eliminate guesswork. The same practice could be followed with the chemicals and galenicals which have the greatest demand. This suggestion is not new, but there are many druggists who have not adopted this practice, who could advantageously do so.

The list below contains examples of inconsistent prescription pricing taken at random from the prescriptions filled by commercial type Store 11-B. They are quite startling when placed side by side on paper, yet occurred frequently in the prescriptions studied in the various drug stores. Of course, in some cases there might be some logical reason for the price discrepancies shown, but as a usual occurrence it would seem strange to charge less for 30 luminal tablets than for 12 of the same tablets. In certain cases the same quantity of a given prescription received different prices, and in other cases the same price was charged, seemingly regardless of the quantity.

One interesting example of careless pricing among many was as follows: The pharmacist was accustomed to receive a four-ingredient prescription calling for 40 capsules, each capsule containing $^1/_2$ grain of luminal. The materials in this prescription cost $0.67, and $1.85 was charged for the prescription. Later the pharmacist received an identical prescription, except the quantity of luminal was 2 grains per capsule. Without bothering to figure out the cost of materials, the pharmacist charged the same price ($1.85) that he had charged for the other prescriptions. However, the increased amount of luminal ran the cost of materials in the prescription up to $1.92, and the pharmacist had thus unknowingly charged less than the cost for the prescription.

It seems that the pharmacist experiences a feeling of reluctance bordering on moral cowardice at charging a sufficiently high price when the materials in a prescription require the prescription to be priced at more than one dollar. For example, it was noted in one store that the pharmacist charged only $1.35 each for a number of prescriptions calling for capsules of glandular products such as corpus luteum which had cost him $1.20. In another case, the pharmacist charged $1.85 for 30 capsules of a certain specialty, which cost him $1.50. At least, some pharmacists seem to take it for granted that a price of one dollar, more or less, will cover the cost and allow a satisfactory profit, but this is by no means true in many cases.

TABLE XV.—EXAMPLES OF INCONSISTENT PRESCRIPTION PRICING.

(From Commercial Type Store 11.)

Description of Prescription.	Quantity.	Selling Price.	
Luminal Tablets	No. 30	$1.10	1.
Identical Prescription	No. 12	1.20	
Calcidine Tablets, gr. 1/3	No. 50	0.90	2.
Identical Prescription	No. 20	0.75	
Identical Prescription	No. 20	0.50	
Identical Prescription	No. 15	0.75	
Capsules Acetyl. Sal. gr. 4, Cod. Sulph. gr. 1/3, each capsule	No. 15	0.90	3.
Identical Prescription	No. 15	1.20	
Capsules Quinine Mur. gr. 3, Luminal gr. 1/2, Thyroid Ext. gr. 1, Cascarine gr. 1/2, each capsule	No. 40	1.45	4.
Identical Prescription	No. 40	1.75	
Identical Prescription	No. 40	2.00	
Argyrol Solution 10%	1/2 oz.	0.35	5.
Identical Prescription	1/2 oz.	0.75	
Identical Prescription	1/3 oz.	0.90	
Identical Prescription	1 oz.	0.35	
S. S. Potassium Iodide	2 oz.	1.25	6.
Identical Prescription	2 oz.	1.45	
Identical Prescription	2 oz.	1.60	
50 Per Cent Solution Potassium Iodide	1/2 oz.	0.90	7.
Identical Prescription	1/2 oz.	0.75	
An Iron Tonic (Manufacturer's Specialty)	2 oz.	1.75	8.
Identical Prescription	4 oz.	1.00	
Identical Prescription	6 oz.	1.35	
Identical Prescription	6 oz.	1.35	
Identical Prescription	8 oz.	1.35	
A Reconstructive Tonic (specialty)	2 oz.	0.75	9.
Identical Prescription	3 oz.	0.75	
Identical Prescription	4 oz.	0.75	
Identical Prescription	4 oz.	1.00	
Elixir Terp. Hyd. and Codeine	3 oz.	1.20	10.
Identical Prescription	4 oz.	1.00	
Identical Prescription	4 oz.	1.25	
Ephedrine Inhalant	1/2 oz.	0.90	11.
Identical Prescription	1 oz.	1.00	
Identical Prescription	1 oz.	1.25	
Fluidextract Ergot	1 oz.	0.60	12.
Identical Prescription	1 oz.	1.00	
Identical Prescription	2 oz.	1.25	

AVERAGE COST OF MATERIALS AND SELLING PRICE OF PRESCRIPTIONS FILLED IN THREE COMMERCIAL TYPE DRUG STORES, BY FORM AND TYPE OF PRESCRIPTION.

The facts presented in Tables XVI, XVII and XVIII are a sample of the information being compiled on the cost and net profit phases of the retail prescription business. It should be kept in mind that the average cost figures shown refer only to the cost of the materials used and do not include cost of containers nor any operating expense, such as the cost of the pharmacist's time, share of rent, and so forth. The prescriptions considered in these tables were filled in commercial type drug stores 4-C, 6-B and 11-B, 3 of the 13 stories studied for the first publication on the prescription department phase of the survey. Store 11-B, with an average charge of $1.03 for all prescriptions, and Store 4-C, with an average prescription price of $1.02, were two of the highest stores in this respect, the average prescription price for all 13 of the commercial type

drug stores being only $0.92. This should be kept in mind in studying these tables, but this fact does not detract from the value of the interesting observations brought out by a perusal of the tables. Store 6-B, however, had an average prescription price of only $0.86.

It is interesting to note that the cost of materials in the average narcotic prescription was less than in the average nonnarcotic prescription in each store. One reason for this is that narcotics are generally prescribed in smaller quantities than are nonnarcotic prescriptions, due to the potency of narcotics and the care with which they must be used Although most narcotics are very expensive per ounce, such a small fraction of an ounce is prescribed that the cost of the narcotic ingredient is usually small. Also, the cost of the nonnarcotic ingredients in the narcotic prescription is often less than in the nonnarcotic prescription, because of the fact that a smaller number of doses is prescribed.

However, it should be noted that there were no specialties among the narcotic prescriptions, which is an important factor in the low average cost of materials in narcotic prescriptions. For example, in Store 11-B, the average cost of materials in nonnarcotic prescriptions was bolstered considerably by the 274 specialty prescriptions, which had an average material cost of $0.45. With specialties excluded, the average cost of materials in nonnarcotic prescriptions in Store 11-B would have been only $0.20, or $0.03 less than for narcotic prescriptions.

In costing these prescriptions, it was noted that the price was generally at quite a premium when purchasing in small quantities. For example, pilocarpine hydrochloride cost $0.46 for 15 grains if purchased in that quantity, but if purchased in 1/8-ounce quantities, 57 grains could be purchased for $0.52. Or, to use an example of an ingredient of more frequent use, acid acetyl salicylic cost $0.15 an ounce if purchased in that quantity, but only $0.08 an ounce if purchased in 1/4-pound lots. Thus, in most cases, an important saving could be made by purchasing in larger quantities. It is wise to purchase no more than necessary of any ingredient of rare occurrence when the extra amount would merely lie idle on the shelves, but with any ingredient which has fairly frequent use, in most cases it would be wise to purchase as large an amount as can be used in a reasonable time to take advantage of the large saving.

The proprietor of Store 11-B was inclined to purchase in very small quantities, smaller than necessary in many cases, thus paying much more for his prescription ingredients than necessary. Thus it was a surprise to find that the average cost of materials in Store 11-B's prescriptions was the same as in Store 6-B, only $0.26, as compared with $0.34 in Store 4-C. However, the prescriptions studied for Store 4-C included 740 specialties with their high average material cost of $0.47, while only 274 specialties are included in the prescriptions filled by Store 11-B. This fact will account for a large part of the difference between the two stores as to cost of materials. (Note also that only 276 specialties were included in the block of prescriptions from Store 6-B.) However, the average cost of materials per prescription was higher in Store 4-C than Store 11-B for every individual type of prescription except mixed prescriptions. Investigation showed, however, that larger average quantities were prescribed in Store 4-C's prescriptions than in the prescriptions filled by Store 11-B. For example, Store 4-C's official nonnarcotic capsule prescriptions called for an average of 20 capsules each, as compared with an average of 17 in Store 11-B. Store 4-C's official narcotic capsule prescriptions called for an average of 26 capsules, as compared with an average of 16 capsules in the same type of prescription in Store 11-B. Store 4-C's official narcotic divided powder prescriptions called for an average of 22 powders as compared with an average of 14 in Store 11-B. Another factor causing the cost of materials to be higher in Store 4-C's prescriptions is that in many more instances than in the case of Store 11-B, the physicians writing Store 4-C's prescriptions prescribed an ingredient under a brand name, rather than under a less expensive U. S. P. or N. F. equivalent.

Some difficulty was encountered in determining cost of materials in the prescriptions studied, due to the fact that it was not possible to tell from the prescription, in some cases, the exact ingredient which had been used. For example, if a prescription called for "acid acetylsalicylic," was this drug dispensed under its chemical name, costing in pound lots approximately $0.07 an ounce, or was a manufacturer's branded product costing $0.81 an ounce used? Similar difficulty was experienced in costing prescriptions calling for luminal, trional, sulphonal and others, the prices of which had a wide range. In the case of luminal, for example, one brand cost $3.45 a half-ounce, and another brand $2.40 a half-ounce.

In one case, the same price was charged for a similar prescription of 30 capsules, whether

acid acetylsalicylic was prescribed under the chemical name or under a brand name. Yet the prescription cost the pharmacist $0.29 more when he used the branded product. This naturally suggests the question of whether the prescriptions containing the branded product were underpriced, or the prescriptions containing the U. S. P. product over-priced. It would seem that this is a subject to be weighed very carefully by practicing pharmacists and students of pharmacy. Daily we read of "get together" meetings held by physicians and pharmacists at which the pharmacists endeavor to interest the physicians in U. S. P. and N. F. products with their marked price advantage over similar products with coined names. Whether or not pharmacists are successful in their undertaking will depend a great deal on whether or not they can convince physicians that a reasonable share of the savings effected are and will be passed on to the patient.

Another situation which developed in the course of costing prescriptions was a case where a pharmacist, due to the price he was charging for the prescription, was obviously using Phenobarbital, U. S. P., although a trade-named equivalent had been prescribed. On inquiry, the pharmacist stated that the physician had authorized him to make this substitution in order to reduce the cost to the patient. The pharmacist thus was able to charge approximately $1.00 less than would have been necessary if he had used the trade-named product. Nevertheless, this is a dangerous practice and may make the pharmacist liable to the manufacturer and lay him open

TABLE XVI.—AVERAGE COST OF MATERIALS AND SELLING PRICE OF 1948 PRESCRIPTIONS FILLED BY COMMERCIAL TYPE DRUG STORE NO. 4-C, BY FORM AND TYPE OF PRESCRIPTION.

Prescription Form.	Type of Prescription. Official. No. of Prescriptions.	Official. Average Cost of Materials.	Official. Average Selling Price.	Mixed. No. of Prescriptions.	Mixed. Average Cost of Materials.	Mixed. Average Selling Price.	Specialties.[1] No. of Prescriptions.	Specialties.[1] Average Cost of Materials.	Specialties.[1] Average Selling Price.
Liquid	397	$0.21	$0.87	368	$0.30	$0.95	361	$0.45	$1.02
Capsules	236	0.20	1.16	45	0.31	1.08	52	0.28	1.16
Tablets	44	0.24	0.83	..	..	..	232	0.43	1.04
Charts	47	0.08	0.83	9	0.27	0.98	4	0.05	1.13
Ointment	17	0.08	0.71	19	0.11	0.77	23	0.52	0.85
Bulk Powder	8	0.11	0.76	4	0.28	0.98	4	0.55	0.96
Effervescent Salt	2	0.33	0.70	..	..	..	57	0.60	1.20
Pills	4	0.16	0.80	..	..	..	4	0.40	1.04
Suppositories	1	0.20	1.25	..	..	..	2	0.50	0.82
Biological	5	2.19	3.20	..	..	..	..	..	..
All Others[2]	1	1.20	0.90	..	..	..	2	0.84	0.90
Total Prescriptions	762	$0.21	$0.96	445	$0.29	$0.96	741	$0.47	$1.05

Prescription Form.	Type of Prescription. Total Narcotics. No. of Prescriptions.	Total Narcotics. Average Cost of Materials.	Total Narcotics. Average Selling Price.	Total Nonnarcotics. No. of Prescriptions.	Total Nonnarcotics. Average Cost of Materials.	Total Nonnarcotics. Average Selling Price.	Total: All Prescriptions. No. of Prescriptions.	Total: All Prescriptions. Average Cost of Materials.	Total: All Prescriptions. Average Selling Price.
Liquid	89	$0.32	$0.99	1037	$0.32	$0.94	1126	$0.32	$0.95
Capsules	142	0.28	1.31	191	0.28	1.05	333	0.28	1.16
Tablets	14	0.33	0.88	262	0.40	1.02	276	0.40	1.01
Charts	4	0.12	1.16	56	0.14	0.85	60	0.14	0.87
Ointment	1	0.18	0.75	58	0.26	0.78	59	0.26	0.78
Bulk Powder	...	..	..	16	0.26	0 86	16	0.26	0.86
Effervescent Salt	...	..	..	59	0.60	1.20	59	0.60	1.20
Pills	...	..	..	8	0.28	0.92	8	0.28	0.92
Suppositories	...	..	..	3	0.56	1.23	3	0.56	1.23
Biological	...	..	..	5	2.19	3.20	5	2.19	3.20
All Others[2]	...	..	..	3	0.96	0.90	3	0.96	0.90
Total Prescriptions	250	$0.30	$1.17	1698	$0.33	$0.97	1948	$0.34	$1.02

[1] There were no narcotic prescriptions among the manufacturers' specialties studied.

[2] All others include (1) medicated soap and (2) ampul prescriptions.

TABLE XVII.—AVERAGE COST OF MATERIALS AND SELLING PRICE OF 1198 PRESCRIPTIONS FILLED BY COMMERCIAL TYPE DRUG STORE 6-B, BY FORM AND TYPE OF PRESCRIPTION.

Prescription Form.	Type of Prescription. Official. No. of Prescriptions.	Official. Average Cost of Materials.	Official. Average Selling Price.	Mixed. No. of Prescriptions.	Mixed. Average Cost of Materials.	Mixed. Average Selling Price.	Specialties.[1] No. of Prescriptions.	Specialties.[1] Average Cost of Materials.	Specialties.[1] Average Selling Price.
Liquid	366	$0.19	$0.77	167	$0.31	$0.94	169	$0.42	$1.01
Capsules	146	0.17	0.95	70	0.27	0.99	16	0.44	1.17
Tablets	78	0.24	0.71	2	0.12	0.62	69	0.42	0.94
Charts	14	0.04	0.74	3	0.12	1.20	3	0.20	0.77
Ointment	47	0.08	0.53	12	0.21	0.87	4	0.31	0.73
Bulk Powder	16	0.12	0.69	..	..	..	8	0.57	1.03
Effervescent Salt	...	..	..	..	..	..	4	0.60	1.23
Pill	...	..	..	..	..	..	..	..	..
Suppositories	1	0.20	1.00	..	..	..	2	0.84	1.25
Ampuls	...	..	..	..	..	..	1	1.06	0.90
Total Prescriptions	668	$0.18	$0.78	254	$0.29	$0.95	276	$0.43	$1.00

Prescription Form.	Type of Prescription. Total Narcotics. No. of Prescriptions	Total Narcotics. Average Cost of Materials.	Total Narcotics. Average Selling Price.	Total Nonnarcotics. No. of Prescriptions	Total Nonnarcotics. Average Cost of Materials.	Total Nonnarcotics. Average Selling Price.	Total: All Prescriptions. No. of Prescriptions	Total: All Prescriptions. Average Cost of Materials.	Total: All Prescriptions. Average Selling Price.
Liquid	77	$0.34	$1.00	625	$0.26	$0.85	702	$0.27	$0.87
Capsules	76	0.22	0.91	156	0.22	1.00	232	0.22	0.97
Tablets	13	0.46	0.83	136	0.31	0.81	149	0.32	0.82
Charts	4	0.10	0.98	16	0.07	0.77	20	0.07	0.81
Ointment	1	0.47	1.00	62	0.12	0.60	63	0.13	0.61
Bulk Powder	...	..	..	24	0.27	0.81	24	0.27	0.81
Effervescent Salt	...	..	..	4	0.60	1.23	4	0.60	1.23
Pills	...	..	..	..	..	..	..	..	..
Suppositories	1	0.20	1.00	2	0.84	1.25	3	0.62	1.17
Ampuls	0	0.00	0.00	1	1.06	0.90	1	1.06	0.90
Total Prescriptions	172	$0.25	$0.95	1026	$0.26	$0.85	1198	$0.26	$0.86

[1] There were no narcotic prescriptions among the manufacturers' specialties studied.

to the criticism of physicians. If the physician wishes the pharmacist to dispense the official product, he should prescribe it as such.

The reader can himself draw some interesting comparisons between official prescriptions and mixed and specialties, between narcotics and nonnarcotics, and between different prescription forms, so it will not be necessary to point them out in this text. Elsewhere in this report, in Table XXXIV, is presented a summary of Store 6-B's prescription department inventory. It is interesting to compare this inventory summary with Table XVII which shows Store 6-B's average prescription cost and selling prices by form and type of prescription.

CHAPTER IV. PRESCRIPTION BUSINESS ACCORDING TO THE PHYSICIANS WRITING THE PRESCRIPTIONS.

A knowledge of his prescription business, according to the physician writing the prescriptions, is of great importance to the pharmacist who wishes to build his prescription business and to operate it in an efficient manner. An exhaustive study of the prescriptions herein analyzed was made from the point of view of the physicians writing the prescriptions. The date of graduation from medical school, the type of practice and the types of prescriptions prescribed were determined for each physician. Prescriptions filled in 1910, 1920 and 1930 were studied, and the business contributed by particular doctors thus traced over a period of two decades. It is believed that this is the first time that an investigation of this type covering all of these factors has been made. There has been a great deal of conjecture concerning preferences of physicians for official

TABLE XVIII.—AVERAGE COST OF MATERIALS AND SELLING PRICE OF 1394 PRESCRIPTIONS FILLED BY COMMERCIAL TYPE DRUG STORE 11-B, BY FORM AND TYPE OF PRESCRIPTION.

Prescription Form.	Type of Prescription. Official. Number of Prescriptions.	Official. Average Cost of Materials.	Official. Average Selling Price.	Mixed. Number of Prescriptions.	Mixed. Average Cost of Materials.	Mixed. Average Selling Price.	Specialties.[1] Number of Prescriptions.	Specialties.[1] Average Cost of Materials.	Specialties.[1] Average Selling Price.
Liquid	485	$0.20	$0.95	297	$0.31	$1.09	143	$0.47	$1.17
Capsules	135	0.11	0.94	61	0.25	1.31	16	0.47	1.36
Tablets	37	0.14	0.96	..	..	..	79	0.43	1.06
Charts	37	0.05	0.80	12	0.08	1.03	6	0.23	1.23
Ointment	27	0.11	0.91	16	0.19	0.98	7	0.36	0.98
Bulk Powder	7	0.20	1.03	..	..	..	5	0.31	0.84
Effervescent Salt	...	..	..	..	..	..	12	0.63	1.18
Pills	3	0.20	1.22	..	..	..	6	0.21	0.76
Suppositories	3	0.81	1.38	..	..	..	..	..	..
Total Prescriptions	734	$0.17	$0.95	386	$0.29	$1.12	274	$0.45	$1.16

Prescription Form.	Type of Prescription. Total Narcotics. Number of Prescriptions.	Total Narcotics. Average Cost of Materials.	Total Narcotics. Average Selling Price.	Total Nonnarcotics. Number of Prescriptions.	Total Nonnarcotics. Average Cost of Materials.	Total Nonnarcotics. Average Selling Price.	Total: All Prescriptions. Number of Prescriptions.	Total: All Prescriptions. Average Cost of Materials.	Total: All Prescriptions. Average Selling Price.
Liquid	92	$0.33	$1.12	833	$0.27	$1.02	925	$0.27	$1.03
Capsules	79	0.14	1.07	133	0.20	1.08	212	0.18	1.08
Tablets	15	0.15	1.22	101	0.36	1.00	116	0.33	1.03
Charts	8	0.05	0.91	47	0.08	0.89	55	0.08	0.89
Ointment	3	0.38	1.13	47	0.16	0.93	50	0.17	0.94
Bulk Powder	...	..	..	12	0.27	0.95	12	0.27	0.95
Effervescent Salt	...	..	..	12	0.63	1.18	12	0.63	1.18
Pills	...	..	..	9	0.20	0.91	9	0.20	0.91
Suppositories	...	..	..	3	0.81	1.38	3	0.81	1.38
Total Prescriptions	197	$0.23	$1.10	1197	$0.26	$1.02	1394	$0.26	$1.03

[1] There were no narcotic prescriptions among the manufacturers' specialties studied.

U. S. P. and N. F. preparations as compared with manufacturers' specialties, and as to whether more recent graduates in medicine show a trend toward more frequent use of the latter. This and other questions concerning physicians' habits in prescription writing are answered in this chapter.

A study of prescriptions will usually show that a small number of physicians account for a large part of the prescription business. The pharmacist should be able to "detail" these few leading physicians without great difficulty, and thus cover the source of much of his prescription business. Study of the type of practice of each of his leading physicians and the types of prescriptions most often written by them should be of value to the pharmacist in planning his inventory. (See remarks made in Chapter VI concerning the importance of close contact with the store's leading physicians in promoting simplification of inventory.)

Table XIX shows the importance of a few physicians out of the many who wrote prescriptions filled by professional Stores A and B. In Store A, 463 physicians wrote the 5474 prescriptions studied. However, the first 10 physicians (ranked according to the number of prescriptions contributed) wrote 35.3 per cent of the prescriptions studied, an average of 193.1 prescriptions per physician. The source of more than half of this store's prescription business could be covered by "detailing" its 25 leading physicians.

The same situation was found in the case of Store B. The first 10 physicians in this store wrote 42.7 per cent of the prescriptions studied, although they accounted for an average of only 149.3 prescriptions each, due to the fact that a smaller number of prescriptions was studied in this store. This pharmacist could cover 65.8 per cent of his prescription business by contacting the leading 25 physicians.

This same information was obtained for eight commercial type drug stores and published in the first prescription department report from this survey. In the case of a chain store unit, the 10 leading physicians accounted for only 21.02 per cent of its prescription business. But in the other seven commercial type stores, all independent retailers, the 10 leading physicians of each store contributed from 43.75 per cent to 89.25 per cent of the total prescription business.

TABLE XIX.—PRESCRIPTION BUSINESS BY PHYSICIANS, GROUPED ACCORDING TO RANK IN NUMBER OF PRESCRIPTIONS WRITTEN.

Store A.				Store B.			
	Number of Prescriptions.		Per Cent		Number of Prescriptions.		Per Cent
Physicians Considered.[1]	Total.	Average per Physician.	of Total Prescriptions.	Physicians Considered.[1]	Total.	Average per Physician.	of Total Prescriptions.
1–10	1931	193.1	35.3	1–10	1493	149.3	42.7
11–25	1157	77.1	21.1	11–25	809	53.9	23.1
26–50	965	38.6	17.6	26–50	605	24.2	17.3
51–100	641	12.8	11.7	51–100	373	7.5	10.6
101–273	590	3.4	10.8	101–150	111	2.2	3.2
274–463	190	1.0	3.5	151–259	109	1.0	3.1
Total	5474	11.8	100.0	Total	3500	13.5	100.0

[1] Physicians are ranked according to the number of prescriptions each wrote among those studied, the physician writing the greatest number being ranked No. 1, etc.

EXTENT TO WHICH PHYSICIANS ARE "DETAILED" BY THE PHARMACIST.

In Stores A and B, no regular "detailing" is undertaken. However, information of interest to physicians in a particular type of practice is passed on to these physicians whenever it comes to the attention of the pharmacists in these stores. Store C "details" physicians to a considerable extent concerning the store in general and not on any particular types of products. Store D also does considerable "detailing" on U. S. P. and N. F. preparations, manufacturers' specialties and products of its own manufacture, with particular emphasis on its own products.

Twenty-two of the questionnaire professional stores detail physicians concerning U. S. P. and N. F. preparations and specialties, while 13 do not. Twenty-nine, or 85.3 per cent of these stores, make personal calls on physicians. Fourteen, or 41.2 per cent, speak before medical groups.

ANALYSIS OF THE PRESCRIPTION BUSINESS OF THE LEADING PHYSICIANS.

Table XX gives more detailed information concerning the 10 leading physicians of both Stores A and B. It is interesting to group the physicians according to the length of the time they have practiced, to see if the doctors who have graduated in more recent years are inclined to prescribe different types of ingredients than the doctors who have been in practice for a long period of time. If there is any decided difference, or "new school" of physicians, the dividing line can undoubtedly be set at the time of the World War. Thus, all doctors who have graduated since 1917 will be considered as "post-war" physicians, and those who graduated prior to 1917 will be referred to as "pre-war" physicians. Differences between the prescriptions of "post-war" and "pre-war" physicians will be pointed out in this chapter whenever such differences are worth noting.

Of Store B's 10 leading physicians, 5 were "post-war" and 5 "pre-war." Of the 5 "post-war" doctors, 3 prescribed more official prescriptions than specialty prescriptions. In analyzing prescriptions it was found that mixed prescriptions contained more official ingredients than specialty ingredients. This fact should be kept in mind in studying the distribution of prescriptions written by these 10 leading physicians. All of the 5 "pre-war" doctors wrote more official prescriptions than specialty prescriptions. In Store A, all but 1 of the 10 leading doctors wrote more official prescriptions than specialties, and this doctor wrote more mixed prescriptions than either official or specialty.

It is interesting to note that all but one of Store B's 10 leading physicians either practiced internal medicine or were dermatologists.

TABLE XX.—BUSINESS FROM FIRST 10 PHYSICIANS IN 1930.

Store A.

Type of Practice.	Year of Graduation.	Number of Prescriptions.	Per Cent of Total Prescription Business.	Per Cent of Total Prescriptions Written. Official.	Mixed.	Specialties.	Private Formula.
Internal Medicine.....	1896	425	7.76	69.9	12.0	17.2	0.9
Dermatology.....	1921	371	6.78	35.5	39.4	3.0	22.1
Internal Medicine.....	1911	238	4.35	9.7	39.9	8.4	42.0
Internal Medicine.....	1923	195	3.56	44.6	39.5	15.9	..
Internal Medicine.....	1897	176	3.22	49.4	19.3	29.6	1.7
Genito-Urinary.....	1909	118	2.16	30.5	39.8	29.7	..
Ophthamology.....	1904	117	2.14	88.0	9.4	2.6	..
General Practice.....	1896	102	1.86	30.4	35.3	34.3	..
Ophthamology.....	1912	96	1.75	60.4	29.2	10.4	..
Ophthamology.....	1908	93	1.70	83.9	14.0	2.1	..
Total.....		1931	35.28	48.2	27.9	14.1	9.8
Total, Not Including Private Formula Prescription.....		1742	33.69	53.5	30.9	15.6	

Store B.

Type of Practice.	Year of Graduation.	Number of Prescriptions.	Per Cent of Total Prescription Business.	Per Cent of Total Prescriptions Written. Official.	Mixed.	Specialties.
Internal Medicine.....	1918	398	11.37	33.2	23.6	43.2
Internal Medicine.....	1896	193	5.52	74.6	14.0	11.4
Dermatology.....	1909	162	4.63	56.1	23.5	20.4
Internal Medicine.....	1919	149	4.26	33.6	25.5	40.9
Internal Medicine.....	1925	123	3.51	46.3	11.4	42.3
Dermatology.....	1900	114	3.26	34.2	56.2	9.6
Internal Medicine.....	1894	97	2.77	55.7	16.5	27.8
Ear, Nose and Throat...	1922	91	2.60	39.5	40.7	19.8
Dermatology.....	1906	83	2.37	48.2	32.5	19.3
Dermatology.....	1928	83	2.37	25.3	55.4	19.3
Total.....		1493	42.66	44.5	26.9	28.6

Professional Store A has been in existence for a considerable period of time, and it was therefore considered of interest to examine some prescriptions filled in previous decades in order to see what, if any, changes have taken place in the passing years. Accordingly, 1000 prescriptions filled in 1910 and 1000 filled in 1920 were examined, and the results of this study, in so far as they regard the physicians writing them, are presented in two tables below.

In Table XXI it will be seen that the 10 leading physicians in 1910 accounted for 54 per cent of the 1000 prescriptions studied, a considerably higher proportion than that accounted for by the first 10 physicians in 1920 and 1930. Detailed information is given in this table for the first 15 doctors. Of these 15 doctors, 10 were recent graduates in 1910, at that time having practiced no more than 15 years. As of interest in showing the extent to which the same doctors remain important to a store's prescription business, the rank of these 15 doctors in 1920 and 1930 is shown, whenever they were still contributing prescriptions in those years. For example, the leading doctor in 1910 ranked third in 1920, and in 1930 after 60 years of practice was still a valuable contributor, ranking forty-first and writing 33 of the prescriptions filled by professional Store A in that year. Again, the doctor who ranked 13th in 1910 and who was at that time a recent graduate, ranked first in both 1920 and 1930, contributing 425 prescriptions in the latter year. On the other hand, another recent graduate in 1910 who ranked second in that year and fourth in 1920, became relatively unimportant to the store's prescription business in 1930 when he contributed only two prescriptions.

TABLE XXI.—STORE A—LEADING PHYSICIANS IN 1910 ON BASIS OF 1000 PRESCRIPTIONS ANALYZED.

Type of Practice.	Date of Graduation.	Number of Prescriptions.	Per Cent of Total Prescriptions.	Rank in 1920.	Rank in 1930.
General Practice	1870	166	16.6	3	41
Dermatology	1900	59	5.9	4	203
Ear, Nose and Throat	1900	45	4.5	5	...
Ear, Nose and Throat	1903	44	4.4	28	57
Ophthamology	1877	42	4.2	35	...
Internal Medicine	1884	39	3.9	..	...
Ophthamology	1883	39	3.9	10	...
Ophthamology	1898	37	3.7	17	...
Surgeon	1898	37	3.7	..	...
Ophthamology	1899	32	3.2	19	13
Sub-total for 10 Leading Doctors..		540	54.0		
Neurology	1898	27	2.7	74	69
Ophthamology	1904	25	2.5	25	7
Internal Medicine	1896	23	2.3	1	1
Ophthamology	1897	23	2.3	14	29
Internal Medicine	1894	20	2.0	9	...
Sub-total for 15 Leading Doctors...		658	65.8		
Other 114 Doctors		342	34.2		
Total		1000	100.0		

TABLE XXII.—STORE A—LEADING PHYSICIANS IN 1920 ON BASIS OF 1000 PRESCRIPTIONS ANALYZED.

Type of Practice.	Date of Graduation.	Number of Prescriptions.	Per Cent of Total Prescriptions.
Internal Medicine	1896	85	8.5
General Practice	1870	46	4.6
Neurology	1886	46	4.6
Dermatology	1900	43	4.3
Ear, Nose and Throat	1900	38	3.8
Ophthamology	1901	30	3.0
Internal Surgery	1900	30	3.0
General Practice	1873	25	2.5
Internal Medicine	1894	22	2.2
Ophthamology	1883	20	2.0
Sub-total for 10 Leading Doctors...		385	38.5
Ear, Nose and Throat	1901	19	1.9
Genito-urinary	1909	19	1.9
General Practice	1888	18	1.8
Ophthamology	1897	17	1.7
General Practice	1894	16	1.6
General Practice	1890	16	1.6
Ophthamology	1898	14	1.4
Ophthamology	1910	14	1.4
Ophthamology	1899	12	1.2
Ear, Nose and Throat	1898	12	1.2
Sub-total for 20 Leading Doctors...		542	54.2
Other 158 Doctors		458	45.8
Total		1000	100.0

It is interesting to note the change in the types of practice of the leading physicians from 1910 to 1930, as this change undoubtedly caused different ingredients and types of prescriptions to be in greatest demand in the different years. Thus the pharmacist should keep himself informed as to his leading physicians, their types of practice and the types of prescriptions and ingredients most frequently prescribed by them in order that his basic prescription department stock can be molded to conform with this changing demand.

Table XXII gives detailed information for the 20 leading doctors in 1920. It will be seen that the 10 leading doctors in 1910 accounted for about the same proportion of the total prescriptions studied as did the 20 leading physicians in 1920. In 1910, 129 physicians wrote the 1000 prescriptions studied, while 178 doctors wrote the 1000 prescriptions studied for 1920. In all three years, 1910, 1920 and 1930, a small number of physicians accounted for a large proportion of the total prescription business. All of the first 10 doctors in 1920 had then been in practice for a considerable period, and this was also true of 8 of the second 10 doctors in 1920.

PREFERENCE OF PHYSICIANS FOR OFFICIAL OR SPECIALTY REMEDIES.

Table XXIII shows the division of the physicians writing the prescriptions studied according to the preponderance of official or mixed and specialty prescriptions among the prescriptions each wrote. The primary purpose in making this tabulation is to verify, if true, the accuracy of the statement so frequently made to the effect that physicians who have graduated since the World War write largely prescriptions calling for specialties, not being taught therapeutics, materia medica and pharmacology to the same extent that physicians graduating before the War were, and thus are more susceptible to the "detail" men representing manufacturers of proprietary specialties. It is well known that these manufacturers have increased in number and their promotional effort multiplied several times. They not only "detail" physicians by sending representatives to call, but they advertise a great deal in medical journals, and mail physicians a considerable amount of literature and samples. In view of these facts, it would not have been surprising to have found the above-mentioned statement verified.

However, the facts in the following table show that both "post-war" and "pre-war" physicians had a preference for official remedies, although "post-war" physicians had a tendency to mix official ingredients with specialties more than the "pre-war" physicians did. This latter tendency may be due to the possibility that "pre-war" physicians are more familiar with official elixirs and syrups used as vehicles and suspension agents, whereas doctors who have graduated in more recent years may be more likely to write for a proprietary form of the same preparation, the proprietary name usually being shorter and easier to pronounce and spell. Considering the funds spent and promotional effort put behind proprietary specialties as compared with official preparations, the fact that both groups of physicians showed a preference for the official form is quite flattering to the official type.

There seems to be little indication that "pre-war" doctors prescribe official remedies to a greater extent than "post-war" doctors. In Store A, a higher percentage of "pre-war" doctors than "post-war" doctors leaned toward official prescriptions, but this was reversed in Store B. In Store A, 53.5 per cent of the "pre-war" doctors prescribed more official remedies than mixed and specialties combined, but this was true for only 44.4 per cent of the "post-war" doctors. In Store B, however, 52.4 per cent of the "post-war" physicians favored official preparations, while the same was true for only 51 per cent of the "pre-war" doctors. In quite a few cases the number of official prescriptions of a physician exactly equalled the combined number of mixed and specialty remedies prescribed, so these doctors were listed under the heading "tie."

In the following table mixed and specialty prescriptions have been considered together and compared with official prescriptions, so that the demand for purely official prescriptions can be seen. It should be remarked, however, that more than half of the ingredients contained in the mixed prescriptions were official ingredients, so the demand for official ingredients is even greater than this table would indicate. This will be seen later in this report where the total number of occurrences of official ingredients and specialty ingredients is shown. For example, if mixed prescriptions are eliminated from consideration in Store B, it is found that of the 55 leading "post-war" doctors, 35 prescribed more official prescriptions than specialties, 15 prescribed more specialties than official and 5 prescribed an equal number of each. Of the 87 leading "pre-war"

doctors in Store B, 55 prescribed more official prescriptions than specialties, 15 more specialties than official and 17 an equal number of each kind.

TABLE XXIII.—TYPES OF PRESCRIPTIONS WRITTEN BY "POST-WAR" AND "PRE-WAR" PHYSICIANS.

Store A.[1]

Physicians Considered.	Type Most Often Prescribed. Official. Number of Doctors.	Official. Per Cent of Total.	Mixed and Specialties. Number of Doctors.	Mixed and Specialties. Per Cent of Total.	Tie. Number of Doctors.	Tie. Per Cent of Total.
"Post-war" Doctors (124)....	55	44.4	55	44.4	14	11.2
"Pre-war" Doctors (260)....	139	53.5	103	39.6	18	6.9
Unknown (79).....	36	45.6	35	44.3	8	10.1
Total (463).....	230	49.7	193	41.7	40	8.6

Store B.[1]

"Post-war" Doctors (84).....	44	52.4	34	40.5	6	7.1
"Pre-war" Doctors (145)....	74	51.0	57	39.3	14	9.7
Unknown (30).....	13	43.3	15	50.0	2	6.7
Total (259).....	131	50.6	106	40.9	22	8.5

[1] Private formula prescriptions not included in this table.

A more detailed picture of the preference of "pre-war" and "post-war" physicians for official remedies as opposed to mixed and specialties is presented in Table XXIV. The doctors are shown in groups according to their rank in the number of prescriptions written by each. The extent of the preference for official prescriptions, or for mixed and specialty prescriptions, is also

TABLE XXIV.—PREFERENCE OF LEADING PHYSICIANS FOR OFFICIAL OR MIXED AND SPECIALTY PRESCRIPTIONS.

Store A.

Type of Prescriptions Written.	Doctors Considered.[1] First 25. Post-war.	First 25. Pre-war.	26–50. Post-war.	26–50. Pre-war.	26–50. Unknown.	51–100. Post-war.	51–100. Pre-war.	51–100. Unknown.	Total: First 100. Post-war.	Total: First 100. Pre-war.	Total: First 100. Unknown.	Total.
100% Official.....	0	0	0	0	0	0	0	0	0	0	0	0
75% Official.....	0	3	1	1	0	1	8	0	2	12	0	14
About Even.....	5	15	1	13	1	8	19	3	14	47	4	65
75% Mixed and Specialties.....	0	2	3	5	0	3	5	1	6	12	1	19
100% Mixed and Specialties.....	0	0	0	0	0	0	2	0	0	2	0	2
Total.....	5	20	5	19	1	12	34	4	22	73	5	100

Store B.

Type of Prescriptions Written.	Doctors Considered.[1] First 25. Post-war.	First 25. Pre-war.	26–50. Post-war.	26–50. Pre-war.	51–100. Post-war.	51–100. Pre-war.	51–100. Unknown.	Total: First 100. Post-war.	Total: First 100. Pre-war.	Total: First 100. Unknown.	Total.
100% Official.....	0	0	1	0	4	0	1	5	0	1	6
75% Official.....	2	4	1	7	3	4	0	6	15	0	21
About Even.....	8	9	5	9	10	17	0	23	35	0	58
75% Mixed and Specialties.....	1	1	2	0	2	5	2	5	6	2	13
100% Mixed and Specialties.....	0	0	0	0	0	2	0	0	2	0	2
Total.....	11	14	9	16	19	28	3	39	58	3	100

[1] The doctors considered are the first 100 in order of importance.

shown. Only the 100 leading doctors in each store are considered, for only these doctors wrote enough prescriptions among those studied to show a possible trend.

From this table it would seem that there is no marked tendency for "pre-war" physicians to prescribe a greater proportion of official remedies than do "post-war" physicians. For example, in the case of Store B, 15 of the "pre-war" doctors prescribed official remedies at least 75 per cent of the time, while 8 other "pre-war" doctors prescribed mixed or specialties 75 to 100 per cent of the time. On the other hand, 11 "post-war" physicians prescribed official remedies 75 to 100 per cent of the time, while 5 other "post-war" doctors prescribed mixed or specialty remedies in 75 per cent of their prescriptions studied.

In Store A, 14 physicians leaned heavily toward official prescriptions, while 21 other physicians wrote mixed or specialty prescriptions most of the time. However, in Store B, 27 physicians wrote official prescriptions at least 75 per cent of the time, and only 15 physicians showed a similar decided preference for mixed and specialties combined. Of the 27 physicians who preferred official prescriptions, 6 wrote official prescriptions in every instance, and 5 of these 6 doctors were "post-war" physicians.

PRESCRIPTION BUSINESS BY TYPE OF PRACTICE OF THE PHYSICIANS WRITING THE PRESCRIPTIONS.

The table below shows the prescription business of two professional pharmacies according to the type of practice of the contributing physicians. In both stores, those physicians who practiced internal medicine predominated, but particularly so in Store B, where doctors practicing internal medicine represented 44.4 per cent of the total number of contributing doctors and wrote 50.2 per cent of the prescriptions studied.

It is interesting to note the major types of practice of the doctors contributing prescriptions to these two stores. Twelve major types of practice are shown. However, the primary reason for including this table is to show the effect of the different types of practice on the demand for official prescriptions, as compared with mixed and specialties. Slightly more than half of the total

TABLE XXV.—PRESCRIPTION BUSINESS BY TYPE OF PRACTICE OF THE PHYSICIANS WRITING THE PRESCRIPTIONS OF TWO PROFESSIONAL PHARMACIES.[1]

Type of Practice.	Physicians.		All Prescriptions.		Prescriptions Written.[3]					
					Official.		Mixed.		Specialties.	
	Number.	Per Cent of Total.	Number.	Per Cent of Total.	Number.	Per Cent.	Number.	Per Cent.	Number.	Per Cent.
Internal Medicine	153	32.8	3072	36.87	1627	53.0	658	21.4	787	25.6
Ophthamology	42	9.0	997	11.96	633	63.5	255	25.6	109	10.9
Dermatology	13	2.8	889	10.67	401	45.1	385	43.3	103	11.6
General Practice	70	15.0	879	10.55	364	41.4	233	26.5	282	32.1
Ear, Nose and Throat	42	9.0	727	8.72	449	61.8	142	19.5	136	18.7
Surgery	32	6.9	552	6.62	282	51.1	88	15.9	182	33.0
Gynecology	30	6.4	333	4.00	144	43.3	64	19.2	125	37.5
Pediatrics	26	5.6	246	2.95	157	63.8	58	23.6	31	12.6
Genito-urinary	12	2.6	196	2.35	55	28.1	60	30.6	81	41.3
Neurology	11	2.4	157	1.88	80	50.9	48	30.6	29	18.5
Cardiology	5	1.1	134	1.61	61	45.5	29	21.7	44	32.8
Diagnostics	2	0.4	77	0.93	37	48.0	27	35.1	13	16.9
All Others[2]	28	6.0	74	0.89	35	47.3	21	28.4	18	24.3
Total	466	100.0	8333	100.00	4325	51.9	2068	24.8	1940	23.3

[1] For Store A, all physicians writing 3 or more prescriptions each are included in this table, plus 13 physicians writing only 2 prescriptions each, but for whom it was possible to ascertain the type of practice. For Store B, all of the 259 physicians writing the prescriptions studied are included in this table.

[2] Includes 14 doctors whose type of practice is unknown but who together wrote 37 of the prescriptions studied, one surgeon and pathologist writing 13 of the prescriptions, a roentgenologist and a proctologist each writing five prescriptions, a pathologist, an orthopedic surgeon, a neurologist-psychologist and an obstetrician each writing 2 prescriptions, two dentists, an endocrinologist, an orthopedic surgeon, a pathologist and a proctologist each writing one prescription.

[3] Private formula prescriptions not considered in this table.

number of prescriptions were official, with the remaining number about equally divided among mixed and specialties. Thus there were more than twice as many official prescriptions as specialties, and for every individual type of practice, except genito-urinary, there were more official than specialty prescriptions. This same situation was true for both stores when considered individually.

LEGIBILITY OF PRESCRIPTIONS.

As pointed out in the report concerning 13 usual commercial type drug stores, prescriptions can be much more efficiently filled if they are written in a good legible hand. Delay, which the customer generally blames on the pharmacist, at times occurs while the pharmacist attempts to get in touch with the prescribing physician to get a translation of a poor specimen of handwriting. Mistakes may easily occur through poor penmanship where two ingredients are fairly alike in name.

In the 13 commercial drug stores, only 3.1 per cent of the prescriptions studied were rated "poor" as to legibility, and the highest proportion of prescriptions with poor legibility for an individual store was 6.3 per cent. It was thought that the above showing for commercial stores was very unfortunate, but the proportion of prescriptions with poor legibility in these professional stores is even higher than the most unfortunate showing for a commercial store.

It would seem from the showing in professional Store A that physicians are less particular about their handwriting to-day than they were two decades ago, although the situation is not quite as bad in that store as it was in 1920. There are a number of ways in which this situation can be remedied. Druggists' associations can contact with physicians through their medical associations, pointing out the advantages which will come to all parties if the physicians will use a little more care in writing prescriptions. The druggist can also "detail" his leading physicians, that small group of doctors who account for a majority of his prescription business, and tactfully put the matter before them, thus obtaining immediate remedial results, in case any of these leading doctors are offenders as to poor penmanship. One manufacturer of specialties with a house organ mailed to physicians has already placed a notice in his publication cautioning physicians to write prescriptions carefully.

TABLE XXVI.—LEGIBILITY OF PRESCRIPTIONS.

	Degree of Legibility of Prescriptions.					
	Good.		Fair.		Poor.	
Store and Date.	Number of Prescriptions.	Per Cent of Total.	Number of Prescriptions.	Per Cent of Total.	Number of Prescriptions.	Per Cent of Total.
Store A (1910).....	245	24.5	722	72.2	33	3.3
Store A (1920).....	149	14.9	767	76.7	84	8.4
Store A (1930).....	1364	24.8	3763	68.4	373	6.8
Store B (1930).....	790	22.6	2420	69.1	290	8.3

THE PROBLEM OF PHYSICIANS' ERRORS IN PRESCRIPTION WRITING.

Quite occasionally while studying the prescriptions filled by the various test stores a prescription was found which quite obviously could not be filled as written. For example, the following is a copy of an actual prescription of this type: Potassium iodide, 2 drams; water, 3 ounces; "Kasagra," 2 ounces; and lithiated sorghum compound, quantity sufficient to make 4 ounces. Obviously, either a larger total quantity was intended or a smaller quantity of one of the other ingredients. In this case, probably the physician intended to prescribe only 3 drams of water. In some cases, however, it was very difficult to determine just what was intended. The pharmacist had undoubtedly called up the physician to determine what he intended to prescribe, and then had filled the prescription correctly, but had failed to note the correction on the prescription. Thus, the pharmacist had no record of the way in which the prescription was filled, for his own protection and convenience in case of a refill. In case the prescription was brought in to be refilled, the pharmacist would either have to call up the physician again, or rely on his memory for the correction, which is not an absolutely safe procedure. Yet a considerable number of such prescriptions were found without any correction noted on the prescription.

Some prescriptions were found which, as a physical possibility, could have been filled as written, but which contained an improper dose of a certain ingredient. For example, one actual prescription called for the following: Acetyl salicylic acid, 4.; codeine sulphate, 3.—capsules No.

15. The physician writing this prescription evidently meant to prescribe "codeine sulphate, .3," as one-sixth of the amount he actually prescribed per capsule would be a large dose. In this and other such cases, the correction was not noted on the prescription. Of course, being a narcotic, there was no question of refills, but for the pharmacist's own protection, particularly in the case of a narcotic prescription, he should have noted the correction on the prescription.

Incidentally, the prescription just given as an example, which could have been filled as written, but which if filled as written might have caused serious harm to the patient if no correction had been made, is an example of the skill, knowledge and experience which the pharmacist must use in filling prescriptions. His work does not consist merely of counting out pills, or pouring liquids from one bottle to another. In addition to the many difficult prescriptions which must be compounded, the pharmacist must have a thorough knowledge of the therapeutic use, effect and dosage of the many hundreds of prescription ingredients which he carries in stock, and must be ever alert to notice errors in prescriptions. No matter how careful physicians are, there are bound to be a certain number of errors in prescription writing, and the trained pharmacist is an additional safeguard in seeing that the patient gets what the physician intended.

(*To be continued next month*)

DIGITALIS IN PHARMACY.

On page 594 of the July JOURNAL a display of Digitalis graphically portrays fields of foxglove, the processing building with the furnace, drying room, and cupboards, cleaning machinery and mill for grinding the dried cleaned leaf to a powder. The exhibit further includes display bottles showing the drug in different stages including the tincture and other products.

Digitalis was selected as a suitable drug for a demonstration of the way in which a common plant is turned to pharmaceutical and medical uses. F. A. Upsher Smith of Minneapolis cooperated with the committee in designing and preparing the digitalis display, which is a very interesting part of the exhibit and a credit to pharmacy.

THE DEPARTMENT OF THE NATIONAL ASSOCIATION OF BOARDS OF PHARMACY

President, A. L. I. Winne, Richmond, Va. *Treasurer*, J. W. Gayle, Frankfort, Ky. *Chairman of Executive Committee*, H. M. Lerou, Norwich, Conn. *Secretary*, H. C. Christensen, 130 N. Wells St., Chicago, Ill.

ACTIVE MEMBER STATES.

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Connecticut	Maine	New Mexico	Utah
Delaware	Maryland	North Carolina	Vermont
D. of Columbia	Massachusetts	North Dakota	Virginia
Florida	Michigan	Ohio	Washington
Georgia	Minnesota	Oklahoma	West Virginia
Idaho	Mississippi	Oregon	Wisconsin
Illinois	Missouri	Pennsylvania	Wyoming
		Porto Rico	

PROGRAM OF THIRTIETH ANNUAL CONVENTION.

NATIONAL ASSOCIATION BOARDS OF PHARMACY, AUGUST 28 AND 29, 1933, HOTEL LORAINE, MADISON, WIS.

MONDAY, AUGUST 28TH, 9:30 A.M.—*First Session.*

1. Call to Order, President Allan.
2. Roll Call.
3. Appointment of Committee on Credentials, President Allan.
4. President's Address, Clare F. Allan.
5. Appointment of Committee on President's Address.
6. Report of Executive Committee, J. A. J. Funk, *Chairman.*
7. Report of Secretary, H. C. Christensen.
8. Report of Treasurer, J. W. Gayle.
9. Presentation of Amendments to Constitution and By-Laws, Duncan Weaver, *Chairman.*
10. Paper: "Accuracy in Compounding as Shown by State Board Examinations," Robert L. Swain.

MONDAY, AUGUST 28TH, 1:30 P.M.—*Second Session.*

1. Report of Legislative Committee, Wm. S. Denton, *Chairman.*
2. Second Roll Call.
3. Appointment of Nominating Committee, President Allan.
4. Report of Advisory Examination Committee, H. C. Christensen, *Chairman.*
5. Report of Syllabus Committee, A. L. I. Winne.
6. Report of Committee on National Legislation, James W. Wise, *Chairman.*
7. Report of Committee on Pharmacy Ownership Law, Geo. W. Mather, *Chairman.*
8. Report of District No. 1, C. Thurston Gilbert, *Vice-President.*
9. Report of District No. 2, Robert P. Fischelis, *Vice-President.*
10. Report of Committee on Banquet Arrangements, O. Rennebohm, *Chairman.*

MONDAY, AUGUST 28TH, AT 6:00 P.M.—*N. A. B. P. Banquet.*

TUESDAY, AUGUST 29TH, 9:00 A.M.—*Joint Session with American Association of Colleges of Pharmacy.*

1. Report of Fairchild Scholarship Committee, E. G. Eberle, *Chairman.*
2. Paper: "Is Compulsory Apprenticeship Registration Working a Hardship on Young Men Entering Pharmacy?" C. B. Jordan, R. W. Sterling.
3. Resolutions from District Meetings, A. F. Schlichting, A. C. Taylor.

TUESDAY, AUGUST 29TH, 2:30 P.M.—*Final Session.*

1. Report of Department of Education, R. L. Swain, *Director.*
2. Report of Committee on President's Address.
3. Report of Publicity Committee, F. D. Pierce, *Chairman.*
4. Report of Committee on Prerequisite Legislation, W. R. Acheson, *Chairman.*
5. Report of Grievance Committee, A. H. King, *Chairman.*
6. Final Report of Credentials Committee.
7. Report of Resolutions Committee, A. C. Taylor, *Chairman.*
8. Report of Committee on Constitution and By-Laws, Duncan Weaver, *Chairman.*
9. Reports of Special Committees.
10. Unfinished Business.
11. New Business.
12. Report of Nominating Committee.
13. Election and Installation of Officers.
14. Adjournment.

COMMITTEE REPORTS

REPORT OF SUB-COMMITTEE ON DIGESTIVE FERMENTS AND GLANDULAR PRODUCTS.*

Three subjects were studied during the past year, whole pituitary substance, trypsin and rennin.

WHOLE PITUITARY POWDER.

It will be recalled that at last year's meeting, a report was made on the oxytocic activity of whole pituitary powder, and that it was voted to re-assay the composite sample this year as well as to prepare and assay a new composite.

This has been done. The composite was prepared, as was last year's, by thoroughly mixing equal weights of whole pituitary powder donated by Armour & Co., Digestive Ferments Co., Eli Lilly & Co., Parke, Davis & Co. and The Wilson Laboratories.

The method of preparing the solution for assay by the collaborators was the same as that used last year.

It was requested that last year's composite sample be re-assayed to ascertain if it had lost any activity.

The results are as follows:

WHOLE PITUITARY POWDER.

Lab.	1933 Sample.	1932 Sample Assayed 1932.	1932 Sample Assayed 1933.
1	160	90	90
2	125	89	87
3	120	80	80
4	125	...	80
5	...	65	65
6	150	100	80
Average	136	85	80

All figures are expressed in international units per Gm.

* Presented at the Twenty-Second Annual Meeting of the American Drug Manufacturers' Association held at Hot Springs, Virginia, May 8–11, 1933.

From the table, it will be seen that the 1933 composite is considerably stronger than the 1932, the average being 136 international units per Gm. as against 85 units for the 1932 composite, as reported last year.

The average of the 1932 composite assayed in 1933 was 80 units as against 85 units last year. Four laboratories report practically identical results for the two years, and the only large variation was that of Laboratory 6. From this, it may be concluded that the 1932 composite has not lost any oxytocic activity in one year.

Why the 1933 composite should be so much stronger than the 1932 is not apparent. Last year, it was agreed to adopt tentatively a value of 75 international units per Gm. In the light of this year's work, it may be desirable to revise this figure. Furthermore, a 1934 composite would add valuable information, as to the variations in strength that could be expected.

The values found by the different laboratories are in excellent agreement considering the nature and limitations of the method. This agreement is due, for the most part, to the use of a standard pituitary powder as a basis of comparison. Without such a standard, it is doubtful if the results would agree so closely. This is an example of the utility of a standard sample, where the method of assay *per se* is subject to wide variations.

It is recommended that

1. A 1934 composite whole pituitary powder be prepared and assayed.
2. The 1932 composite be re-assayed to determine its further keeping qualities.
3. The definition for whole putuitary powder adopted last year be tentatively changed to read as follows:

> Whole pituitary powder, derived from cattle, swine or sheep, shall contain not less than 100 international units per Gm.

TRYPSIN.

Last year, an A. D. M. A. reference trypsin was adopted tentatively, with the recommendation that it be re-assayed this year. Eight laboratories collaborated.

The methods of assay were the same as employed last year, *viz.*, the U. S. P. X method and the Smith-Sorensen method. The results are shown in the following table:

TRYPSIN.

Lab.	U. S. P. Method, 1933.	Smith-Sorensen, 1933.	U. S. P. Method, 1932.	Smith-Sorensen, 1932.
1	20.0	23.6	25.0	25.0
2	32.0	26.8	35.0	23.5
3	26.3	28.0	37.5	35.8
4	25.0	26.3	25.0	26.3
5	23.8	23.9	25.0	25.6
6	30.0	31.8	25.0	25.8
7	25.0	34.0	25.0	26.9
8	33.0	36.3	33.3	37.5
Average	26.9	28.8	28.8	28.3

The figures mean the number of parts of casein digested by one part of the trypsin.

It will be noted that the average strength by the U. S. P. method in 1932 was 28.8, whereas this year it is 26.9; by the Smith-Sorensen method 28.3 in 1932 and 28.8 in 1933. This would indicate that the reference trypsin had not undergone any serious deterioration, if any, during the past year.

Comments by various laboratories are worthy of mention.

Laboratory 1.

> "It will be noted that the reference sample has shown deterioration and that the U. S. P. X method indicates a greater loss in potency than does the modified Smith-Sorensen method.
>
> "Our experience leads us to believe that trypsin is distinctly unstable.

"We believe that the modified Smith-Sorensen method appears the means of providing a standard assay procedure, at least until something better is proposed. For instance a sample of trypsin requiring not less than 2 cc. of exactly $N/20$ sodium hydroxide solution would be considered to meet the U. S. P. requirement."

Laboratory 3.

"We re-assayed the six samples that had been used to make up this reference standard, and I give you below the comparative tests on all six as made in 1931 and again as recently retested.

	U. S. P. Method.		Smith-Sorensen Method.	
	(1931) Per Cent.	(1933) Per Cent.	(1931) Per Cent.	(1933) Per Cent.
No. 1	120	110	112	122
No. 2	100	85	123	112
No. 3	105	90	100	86
No. 4	110	105	98	101
No. 5	105	110	128	127
No. 6	100	90	100	91

"From these results it will be observed that the two methods check very closely in regard to deterioration of samples with the exception of No. 2. In samples Nos. 3 and 6 there appears to be about a 10 per cent loss in activity."

Mr. Taylor calls attention to a lack of preciseness in the directions of the U. S. P. method, with regard to the time that should elapse between the removing of the tubes from the bath and the adding of the acetic acid-alcohol mixture. Also, that there is no specification of temperature to which the tubes should be cooled before adding the acid-alcohol mixture. Both of these factors affect the accuracy of the end-point.

"There is a point to be observed in regard to the Smith-Sorensen method that has to do with adjustment of the hydrogen-ion concentration. From our experience we do not believe phenol red a satisfactory indicator for adjustment of casein solutions. In the work we did on this particular method several years ago we tried phenol red and could not obtain satisfactory results, so we carried out our adjustments using brom thymol blue and thymol blue as indicators. We were able in this way to adjust solutions to a definite p_H colorimetrically which we were able to check almost perfectly by potentiometric means."

Mr. Willson, of Parke, Davis & Co., is working on the details of a revised simplified method of preparing the casein solution. This would be a big advantage, since the present method of making the casein solution for the Smith-Sorensen method is time-consuming, and is the main objection to the method.

Mr. W. H. Blome called attention to an uncertainty in the directions for making up the casein solution for the Smith-Sorensen method, in that a 4 per cent solution could not be obtained if the final volume was as directed and no allowance made for the portions of the solution used to determine the p_H. Inquiry among the collaborators disclosed that practically all of them had recognized the discrepancy and had made up the final solution on a 4 per cent basis.

The Smith-Sorensen method appears to be gaining favor among the collaborators. It has the advantage over the present U. S. P. method of greater preciseness of end-point, and would not require a standard reference trypsin.

RECOMMENDATIONS.

It is recommended that

1. The present study of the A. D. M. A. reference trypsin be continued.
2. The Smith-Sorensen method be studied more critically with a view to simplifying it, and ascertaining its accuracy.
3. The U. S. P. Revision Committee be asked to postpone final action on pancreatin as long as possible, so that the A. D. M. A. may study certain improvements in the methods of assay.

RENNIN.

This year's work consisted of a further study of the keeping qualities of the A. D. M. A. reference rennin. The collaborators were asked to test the rennin by the National Formulary Fifth Edition Method.

The results are contained in the following table:

RENNIN.

Lab.	Time of Coagulation (Minutes).	Milk.	Acidity before Adjustment (Per Cent).	Acidity after Adjustment.
1	9.5	Certified	0.144	Not adjusted
1	10.0	Pasteurized	0.140	Not adjusted
2	9.5	Pasteurized	0.140	0.146
3	11.75	Pasteurized	0.142	Not adjusted
4	11.16	Pasteurized	0.145	Not adjusted*
4	11.75	Pasteurized	0.145	Not adjusted†
4	10.42	Pasteurized	0.145	Not adjusted‡
5	10.5	Grade A Raw	0.144	Not adjusted
6	10.25	Pasteurized	0.144	Not adjusted
7	11.5			0.147
8	12.25	Grade A	0.165	Not adjusted
8	22.0	Grade A	0.165	0.150

*Milk two days old. † Milk one day old. ‡ Milk four hours old.

Laboratory No. 1 comments,

"Two reference samples submitted to us in October of 1928, have also been re-assayed at this time and have shown no appreciable deterioration.

"Our experience indicates that rennin is stable over a period of years. We would recommend that a standard rennin be adopted."

Laboratory No. 3 states,

"We have had a peculiar experience in retesting the A. D. M. A. reference rennin according to the National Formulary 5th Edition Method. Our first test was as follows:

Curdling time: 17 minutes 5 seconds.
Kind of milk: Pasteurized.
Acidity: 0.141 per cent lactic acid (no adjustment).

"This result on curdling time is much different from results obtained during the past several years using this same sample. The curd obtained instead of being firm as it usually is, was stringy. We attributed this slowness in curdling to the sample of milk used although its acidity was almost exactly that which is desired and there was no adjustment of acidity by addition of alkali. Subsequently we obtained another quantity of milk from the same dairy and the test on the standard rennin results as follows:

Curdling time: 11 minutes 45 seconds.
Kind of milk: Pasteurized.
Acidity of milk: 0.142 per cent lactic acid (unadjusted).

"The first test above is the first one in several years of testing that has been outside the limits of 9 minutes to 13 minutes curdling time. Usually we have been able to blame variations of curdling time upon variations in acidity and especially attempts to adjust the acidity artificially. In this case these factors are not involved but it appears that this is one more fact indicating that variation in milk supplies sometimes unknown may very materially affect the result of the rennin test.

"We have made it a rule not to use for the test any milk that exceeded an acidity of 0.15 per cent calculated as lactic acid and we have abandoned altogether any idea of adjusting milk that is more acid by adding sufficient alkali. If the milk is not naturally at the proper acidity, we do not use it.

"I am decidedly of the opinion that in the next revision of the National Formulary adjustment of the milk by the addition of alkali should be omitted but that preferably a test for acidity should be included and milk that runs more than 0.15 per cent acidity as lactic acid should not be used.

"Of course, with a reference standard for direct comparison it does not make so much difference if the acidity varies somewhat and the adoption of such a standard would help to eliminate the errors that may occur due to variations in sources of supply of milk."

Laboratory No. 4 states,

"These tests indicate that, compared with the laboratory test last year, this rennin standard has decreased slightly in activity."

Laboratory No. 5 concludes that the standard rennin "curdles the milk in slightly less time than we reported last year." This laboratory also makes the suggestion that the titration for acidity can be made more sensitive, if five drops of the milk being titrated be added to 5 cc. of water. The pink color shows up better. It is customary to use 50 cc. of the milk, to which 0.5 cc. of phenolphthalein solution has been added. After the preliminary titration a second one should be made using just a little less than expected amount of alkali.

Laboratory No. 6 remarks that this year's results "are very close to those which we reported last year."

This year's work confirms the previous conclusion that the National Formulary Fifth Edition Method is unsatisfactory and unreliable, and that a standard rennin would overcome the difficulties inherent in the present method. The work adds another year's cumulative evidence for the excellent keeping quality of the A. D. M. A. reference rennin and its suitability as a standard in case a method based upon the use of a standard is adopted in the National Formulary Sixth Edition.

RECOMMENDATIONS.

It is recommended that,

1. The study of the keeping quality of the A. D. M. A. reference rennin be continued.
2. On behalf of the American Drug Manufacturers' Association, a revised method for the assay of rennin be submitted to the National Formulary Sixth Edition Revision Committee. Such method will make use of a standard rennin and will omit adjustment of the acidity of the milk.

In conclusion, I want to express my very sincere appreciation to the members of the committee for their splendid collaboration during these many years. It is hoped that their efforts will result in improved methods of assay in the forthcoming editions of the United States Pharmacopœia and of the National Formulary.

DAVID KLEIN, *Chairman*,
W. H. BLOME,
H. A. B. DUNNING,
B. TAPPEN FAIRCHILD,
FREDERIC FENGER,
HOWARD T. GRABER,
F. W. HEYL,
H. W. RHODEHAMEL,
F. O. TAYLOR,
D. M. FINDLAY.

DETERMINATION OF TAUROCHOLIC ACID IN BILE SALTS.*

F. E. WILLSON.

The bile contains as its chief constituents, taurocholic acid and glycocholic acid. These generally occur as the sodium salts and are not to be found in the pancreatic juice or in any of

* Presented at the Twenty-Second Annual Meeting of the American Drug Manufacturers' Association held at Hot Springs, Virginia, May 8–11, 1933.

the normal animal secretions other than the bile. Their function in the bile is to emulsify fats and assist in the absorption of fatty acids. In this way they are material aids to digestion. These acids may be present in the bile in varying proportions depending upon the animal source and the general metabolism of the animal. Besides these two acids there may be present other analogous substances such as taurocholeic acid and glycocholeic acid. It is generally agreed these are present in very small amounts, if at all, and are therefore worthy of little consideration.

The problem of obtaining a satisfactory method for the determination of the relative amounts of taurocholic acid and glycocholic acid has been a matter of investigation for a number of years. At first, the chief interest in this respect was the determination of the two acids in bile, itself, so that the results might be used in conjunction with certain clinical observations. When these two important constituents of the bile were made available commercially in the form generally known as bile salts the demand for methods of determinination become even more a matter of interest and investigation.

The methods for the determination of the taurocholic acid content of bile and mixtures of bile salts are based principally upon its sulphur content since taurocholic acid contains sulphur while glycocholic acid does not. Some of the earlier investigators attempted to use a method based upon a difference in solubility of the two acids with a subsequent amino nitrogen determination. Foster and Hooper (1) suggested such a method in which the taurocholic acid fraction was hydrolyzed with sodium hydroxide into taurine and cholic acid. The amino acid content of the taurine was then determined by the Van Slyke method. A later method (2) used a similar line of procedure but besides determining the amino nitrogen of the taurine, the sulphur content was also determined and the two used in conjunction in calculating results. The same investigators elaborated on this method in a later communication (3) and suggested that the Asboth-Dunning method for determining the sulphur content be used. Many other methods are to be found by reference to the literature but in principle most of them follow along the same lines. Since most of these earlier methods were for the determination of taurocholic acid in the bile, itself, there was a tendency to separate it from the glycocholic acid by means of solvents. These methods gave unsatisfactory results because the differences in solubilities made use of did not entirely exist. Also, Hammersten showed that in many samples of bile there were present certain ethereal sulphates and sulpholipins that possessed the same solubilities as did taurocholic acid. Therefore, any method using the sulphur content for calculating the amount of taurocholic acid in bile would give erroneous results if these substances were present. In the commercial product, marketed as bile salts, we are not confronted with this problem since the methods of preparation practically exclude the ethereal sulphates and sulpholipins. Therefore our chief problem from a commercial standpoint is to obtain some satisfactory method for determining sulphur in organic combination in a product of this kind. From this determination the taurocholic acid content then can be calculated.

Several years ago the Sub-Committee on Digestive Ferments and Glandular Products of the American Drug Manufacturers' Association adopted for study the bile salts. Dr. Kirk submitted methods (4) for determining both glycocholic acid and taurocholic acid. The method for determining taurocholic acid was based upon a sulphur determination using the Hoffman-Gortner method (5). On giving this method a trial in a number of different laboratories it was found that extremely divergent results were obtained. The taurocholic acid content of the particular sample under investigation was found to range anywhere from 30 per cent to 49 per cent. This indicated that the method was unsuitable for analytical purposes. This wide range of results appeared to us as being due to the fact that complete oxidation of the sulphur was not insured. The method had a further disadvantage in that it required a considerable length of time to carry it out. This is a point that must be considered in routine analytical work.

Since there were two serious objections to the Hoffman-Gortner method applied to bile salts it seemed that there should be some other available method for use. For that reason a search was made for methods and the ones that showed promise of meeting the two requirements were given a trial. The method which gave consistent results and at the same time was rapid in manipulation was one employing the Parr Sulphur Bomb. Following is an outline of the method devised for its use as applied to bile salts:

Procedure.—A 1-Gm. sample of bile salts is weighed into the ignition cup of a Parr Sulphur Bomb. One Gm. of potassium chlorate and 10 to 15 Gm. of sodium peroxide, followed by 0.2

Gm. of benzoic acid, are added. After covering the ignition cup with the top equipped with the ignition wire the whole is sealed in the bomb by means of the screw-cap. The bomb is then well shaken to insure uniform mixing of the contents. The contents are then ignited in the usual manner using an electric current. After ignition the bomb is cooled, the ignition cup together with the separated top is placed in a 600-cc. beaker. About 250 cc. of distilled water is then added and the fusion mixture brought into solution with the aid of heat. After complete solution the ignition cup and top are removed, washing well with distilled water. The solution is then carefully acidified with hydrochloric acid. After an acid reaction has been reached the solution is filtered and the sulphur determined in the filtrate preferably by the gravimetric method using barium chloride solution. The amount of sulphur found multiplied by 16.07 gives the amount of taurocholic acid present in the sample.

If the gravimetric method is used the sulphur is in combination as barium sulphate and must be calculated from the weight of the precipitate obtained. The conversion factor 16.07 is obtained by considering taurocholic acid to have the formula $C_{26}H_{45}NSO_7$ with a molecular weight of 515.45.

The reagents used in this method must necessarily be first tested for sulphur and found to be sulphur free.

Determinations by this method may be carried out rapidly. The preparation and ignition of the sample requires only about 20 minutes while the sulphur determination ordinarily requires about 2 hours. This is a considerable advantage over the Hoffman-Gortner method which generally requires several days to carry to completion.

The proposed method also has the added advantage of carrying the oxidation to completion. This probably can be best illustrated by comparison of results obtained by the Hoffman-Gornter method and this Parr-Bomb method.

	Hoffman-Gortner Method.	Parr-Bomb Method.
Determination No. 1.....	32.90% taurocholic acid	38.92% taurocholic acid
Determination No. 2.....	33.89% taurocholic acid	41.22% taurocholic acid
Determination No. 3.....	37.89% taurocholic acid	42.59% taurocholic acid
Determination No. 4.....	33.22% taurocholic acid	42.33% taurocholic acid

It will be observed from the above results that lower results are obtained by the Hoffman-Gortner method. This would be indicative that complete oxidation of the sulphur is not reached. With the Parr-Bomb method there was some variance in results but when it is considered that the conversion factor from sulphates to taurocholic acid is high (16.07) these results would be expected.

The Parr-Bomb method has been used with considerable success in this laboratory since its submission to the A. D. M. A. The following table contains the results of the analyses of four different samples of bile salts which are representative of results that may be expected:

Sample No. 1.....	I.	38.04% taurocholic acid
	II.	40.37% taurocholic acid
	III.	38.84% taurocholic acid
Sample No. 2.....	I.	40.73% taurocholic acid
	II.	41.36% taurocholic acid
	III.	40.89% taurocholic acid
Sample No. 3.....	I.	47.19% taurocholic acid
	II.	47.58% taurocholic acid
	III.	46.53% taurocholic acid
Sample No. 4.....	I.	47.23% taurocholic acid
	II.	47.69% taurocholic acid
	III.	47.76% taurocholic acid

In working with bile salts, we believe the Parr-Bomb method will give more accurate and reliable results for the sulphur content than any of the other available methods. Consequently a truer evaluation of taurocholic acid will be obtained. If the method were applied to bile a special preparation of the sample would have to be first carried out in order to exclude any of the other sulphur-containing substances, other than taurocholic acid, being present.

LITERATURE CITED.

(1) Foster and Hooper, *J. Biol. Chem.* (1919), 355–366.
(2) Rosenthal and Falkenhausen, *Arch. exptl. Path. Pharmakol.*, 98 (1923), 321–338.
(3) Rosenthal and Falkenhausen, *Klin. Wochschr.*, 2 (1923), 1111–1114.
(4) Proceedings of the American Drug Manufacturers' Association (1929).
(5) Hoffman and Gortner, *J. A. C. S.*, 45 (1923), 1033.

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1932–1933.

Office of the Secretary, 10 West Chase St., Baltimore, Md.

LETTER NO. 10.

July 26, 1933.

To the Members of the Council:

70. Tentative General Program for the Eighty-First Annual Meeting. Motion No. 20 (Council Letter No. 9, page 663) has been carried and the tentative general program is approved. Local Secretary Stanley and his associates have been advised and copies of the program have been sent to the pharmaceutical press.

71. Authorizing Dr. Hilton to Sign Checks in the Absence of Treasurer Holton. Motion No. 21 (Council Letter No. 9, page 663) has been carried and the approved banks of deposit have been advised of the authority granted to S. L. Hilton in the absence of C. W. Holton.

72. Research Award. Motion No. 22 (Council Letter No. 9, page 664) has been carried and Dr. Husa has been advised.

73. Contract for Printing and Distributing the Year Book, Volumes 20 and 21. Motion No. 23 (Council Letter No. 9, page 664) has been carried and the contract for printing and binding the YEAR BOOK, Volumes 20 and 21, in one binding has been awarded to the Lord Baltimore Press, Baltimore, Md.

74. Applicants for Membership. Motion No. 24 (Council Letter No. 9, page 664) has been carried and applicants for membership numbered 161 to 173, inclusive, have been elected to membership.

75. Contract for Printing and Binding the National Formulary VI. Recently Chairman DuMez issued the following bulletin to the members of the Committee on Publications:

"After consultation with Chairman Gathercoal of the Committee on National Formulary as to the progress of revision and in view of the possibility of increases in cost, invitations were sent out recently to the firms which might be interested to submit bids on the cost of printing and binding the N. F. VI.

"Bids were received from the J. B. Lippincott Company, Philadelphia, Pa., the Lord Baltimore Press, Baltimore, Md., and the Mack Printing Company, Easton, Pa. The estimates of these three firms were carefully checked and that submitted by the Mack Printing Company was found to be the most favorable. This bid will result in decided reduction in the cost of the book over that of the N. F. V. It is estimated that there will be a saving of between $5000 and $6000 on the first series of 25,000 copies. Approximately 45,000 copies of the N. F. V have been printed and if the sale of the N. F. VI compares, there will be a total saving of from $10,000 to $12,000. Of course, the amount cannot be definitely stated as the contract calls for an adjustment for labor and materials on the basis of existing conditions, at the time later series may be printed.

"Inasmuch as the Mack Printing Company handled the work satisfactorily for the N. F. V, and as this firm has now had the experience of printing one edition of the National Formulary, and as their bid is the most favorable, it is suggested that it be recommended to the Council of the AMERICAN PHARMACEUTICAL ASSOCIATION that the contract for printing and binding the N. V. VI be awarded to the Mack Printing Company."

The following communication has just been received from Chairman DuMez:

"A majority of the members on the Publication Committee have voted in favor of the

Mack Printing Company with respect to the printing of the N. F. VI.

"It is, therefore, recommended to the Council that the contract for the printing and binding of the National Formulary VI be awarded to the Mack Printing Company of Easton, Pa., on the basis of the estimate submitted."

(*Motion No. 25*) *It is moved by DuMez that the contract for printing and binding the National Formulary VI be awarded to the Mack Printing Company, Easton, Pa., on the basis of their estimate, and that the President and Secretary of the Association be authorized to sign the contract.*

76. Joint Membership Fee with the N. A. R. D. and the State Pharmaceutical Associations. The following communication has been received from the Maryland Pharmaceutical Association:

> "At the recent annual meeting of the Maryland Pharmaceutical Association, the following resolution was adopted:
>
> " '*Resolved* that the Maryland Pharmaceutical Association concur in the suggestion of President Kantner that the Council of the AMERICAN PHARMACEUTICAL ASSOCIATION and the Executive Committee of the National Association of Retail Druggists be urged to confer for the purpose of working out some coöperative plan whereby membership in the state associations will carry with it membership in both national organizations.' "

Chairman Hilton has advised that this proposal be included in this letter for the information of the members of the Council, and that it be considered at the joint meeting of the Council with the Executive Committee of the N. A. R. D. on Wednesday, August 30th, at Madison. Secretary Henry of the N. A. R. D. agrees that this is a proper subject for discussion at the joint meeting.

77. Life Membership. Theodore D. Wetterstroem, Columbus, Ohio, has become a Life Member of the ASSOCIATION through the payment of dues for thirty-seven consecutive years.

78. Use of Text of N. F. V. The following communication has been received from Samuel M. Gordon, Secretary, Council on Dental Therapeutics, American Dental Association:

> "The Council on Dental Therapeutics, of the American Dental Association, is planning to run serially in *The Journal of the American Dental Association*, and subsequently reprinted in book form, a series of articles on drugs useful in dentistry. In character, the book will be a combination of *Useful Drugs* and *New and Nonofficial Remedies* of the American Medical Association.
>
> "Included in the book will be, of course, comments on parts of the *National Formulary*, Fifth Edition. Permission to use for comment such parts is requested. It is, of course, understood that any such comments or quotations from the *National Formulary* will be made solely on the responsibility of this Council. It is hoped that this permission can be obtained."

Chairman DuMez of the Committee on Publications recommends that permission be granted to use for partial reproduction the text of the N. F. V, and that in this instance the permission be granted without charge.

(*Motion No. 26*) *It is moved by DuMez that permission to use the text of the N. F. V for partial reproduction in a series of articles on drugs useful in dentistry, to run serially in the Journal of the American Dental Association and subsequently be reprinted in book form, be granted to the Council on Dental Therapeutics of the American Dental Association without charge upon condition that there be placed upon the reverse of the title page of the booklet the usual acknowledgment.*

79. Applicants for Membership. The following applications properly endorsed and accompanied by the first year's dues have been received:

No. 174, William M. Armstrong, Jr., 2167 E. Cumberland St., Philadelphia, Pa.; No. 175, Theodore Campbell, Jr., 63rd St. & Overbrook Ave., Philadelphia, Pa.; No. 176, Laomie Gilbert, Jr., Benson, N. C.; No. 177, M. C. Kaegi, North Pacific College of Oregon, Portland, Oreg.; No. 178, Lillian Mary Langevin, 3117 So. 16th St., Lincoln, Nebr.; No. 179, John Andrew Lynch, 2132 N. 9th St., Philadelphia, Pa.; No. 180, Orville McLaughlin, City Drug Store, Pawnee, Okla.; No. 181, John Russell Mason, George Washington University Library, 2023 G St., N. W., Washington, D. C.; No. 182, Harry A. Mikkola, 318 Sherman Ave., Evanston, Ill.; No. 183, Harold E. Repass, R. R. No. 2, Carmel, Ind.;

No. 184, Leonard Dale Seif, 5919 Wyatt Ave., Cincinnati, Ohio; No. 185, Sister Beatrice Martin, St. Leo's Hospital, Greensboro, N. C.; No. 186, Sister Margaret Mary McCarthy, St. Mary's Hospital, Saginaw, Mich.; No. 187, Chas. E. Smyithe, 710 S. E. 14th Ave., Minneapolis, Minn.; No. 188, Asa N. Stevens, 37 Johnson Ave., Indianapolis, Ind.

(*Motion No. 27*) *Vote on applications for membership in the American Pharmaceutical Association.*

E. F. KELLY, *Secretary.*

LOCAL COMMITTEES FOR A. PH. A. MEETING.

Local Secretary, Emerson D. Stanley. **Convention Committee:** *Chairman*, Oscar Rennebohm, A. F. Menges, Edward J. Ireland, Franklyn J. Bergman; *Treasurer*, Emil A. Hayden; *Secretary*, Charles C. Charmley. **Chairmen of Sub-Committees:** *Women's*, Mrs. A. F. Menges; *Entertainment*, Richard Weiss; *Hotels*, E. G. Kuenzi; *Publicity*, Ralph W. Clark; *Registration*, Arthur H. Uhl; *Transportation*, R. J. Tiedeman. **Chairmen of Affiliated Associations:** *American Association Colleges of Pharmacy*, Miss Nellie A. Wakeman; *National Association Boards of Pharmacy*, Oscar Rennebohm; *National Conference Pharmaceutical Research*, Arthur H. Uhl; *Plant Science Seminar*, W. O. Richtmann; *Conference of Pharmaceutical Association of Secretaries*, Ralph W. Clark; *Conference of Pharmaceutical Law Enforcement*, Harry Klueter. **Women's Committee:** *Chairman*, Mrs. Adolph F. Menges; **Chairmen of Sub-Committees:** Mrs. Wilbur Beache, Mrs. Charles Charmley, Mrs. Ralph Clark, Mrs. Andrew Helstrom, Mrs. Edward Kremers, Mrs. Harry Leonard, Mrs. Oscar Rennebohm, Mrs. W. O. Richtmann, Mrs. Emerson D. Stanley, Miss Nellie Wakeman.

TRANSPORTATION AND RATES TO MADISON.

On account of the Century of Progress exposition, greatly reduced rates to Chicago are in effect from every part of the country—as low as one fare plus 25 cents for the round trip and slightly higher rates with a longer return limit.

The Committee on Transportation of the A. PH. A. has secured a reduced round-trip rate of one and one-third fare to Madison on the identification certificate plan good for thirty days. Tickets on this plan will be on sale as early as August 14th, in distant territories.

However, it is suggested: (1) That members buy the best special excursion ticket to Chicago they can get and use the identification certificate to buy round-trip ticket from Chicago to Madison; (2) members whose route to Chicago is through Madison should buy the best special excursion ticket to Chicago and obtain stopover at Madison for the meeting.

The round-trip fare to Madison at the one and one-third certificate rate is $6.25.

A TRIP TO THE DELLS OF THE WISCONSIN RIVER.

RALPH W. CLARK.

Arizona has its Grand Canyon, and the Hudson its Palisades. Mention of Northern Wisconsin, Michigan and Maine brings visions of towering pines, big woods and countless lakes. Pinehurst, French Lick and White Sulphur Springs invite the wealthy to days of leisure, golf and rest. . . Nowhere can you find all of these things so beautifully blended and to be enjoyed so well as in the Wisconsin Dells.

Here, nature has assembled in miniature the beauties and grandeur of our country's scenic masterpieces. Here you will find the "grand canyon" of the Wisconsin River—not unlike its big brother in the West. Towering, pine-covered palisades, lofty crags and fantastic rock formations frame in primitive glory the dark waters of the Wisconsin that for ages have carried a breath of mystery and adventure from the far north. . .

The far-flung hills of the Dells region are heavily wooded. Pine trees and hemlock, birch and hardwoods, with a sprinkling of jewel-like lakes, bring to you a true taste of north woods splendor.

Romantic, adventurous, scenic, historic, the Wisconsin Dells may be visited by those attending the Madison convention. This trip through sixty miles of beautiful Wisconsin, followed by a three-hour boat trip on the river will be available, without cost, except for meals, on September 2nd.

PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and Branches shall become the property of the Association with the understanding that they are not to be published in any other publication prior to their publication in those of the Association, except with the consent of the Council." —Part of Chapter VI, Article VI of the By-Laws.

ARTICLE III of Chapter VII reads: "The objects and aims of local branches of this Association shall be the same as set forth in ARTICLE I of the Constitution of this body, *and the acts of local branches shall in no way commit or bind this Association, and can only serve as recommendations to it.* And no local branch shall enact any article of Constitution or By-Law to conflict with the Constitution or By-Laws of this Association."

ARTICLE IV of Chapter VII reads: "Each local branch having not less than 50 dues-paid members of the Association, holding not less than six meetings annually with an attendance of not less than 9 members at each meeting, and the proceedings of which shall have been submitted to the JOURNAL for publication, may elect one representative to the House of Delegates."

Reports of the meeting of the Local Branches shall be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten with wide spaces between the lines. Care should be taken to give proper names correctly and manuscript should be signed by the reporter.

DETROIT.

The Pharmaceutical Conference, in conjunction with the May meeting of the Detroit Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION, was held in Ann Arbor, May 11, 1933. The Conference was opened by Dean Edward H. Kraus of the College of Pharmacy of the University of Michigan, who acted as chairman.

Dr. Alexander G. Ruthven, president of the University of Michigan, welcomed the pharmacists of Michigan to Ann Arbor and invited them to make use of the University which belongs to the people of Michigan.

Dean Kraus arranged a splendid program for the day, the speakers were selected from the faculty of the University. The subjects were so diversified that virtually a postgraduate course was obtained by the large gathering.

The first speaker on the program was Dr. Charles W. Edmunds, professor of materia medica and therapeutics in the medical school. Dr. Edmunds spoke on "Drug Addiction, a World Problem." He presented some interesting and startling figures on drug addiction. The Island of Formosa has a law making it compulsory to cure addiction. Turkey and Syria present the problem of smuggling. In 1931 alone four tons of heroin were seized at the wharves while 11,650 kilos were seized inside the country.

The chief source of opium has been China, but owing to the unsettled condition of that country Japan has become the source of manufacture. However, addicts are few in that country. India uses a decoction of poppy capsules known as "Post" and is used as a beverage which is even fed to the young. The last opium auction held in Calcutta was in 1926. Egypt, with an adult population of 300,000, presents a real problem; one in ten use hashish, 100,000 use opium and 54,000 are addicts to heroin.

France at one time had 325 factories manufacturing narcotics. Since the last conference she has reduced them to 15; the illicit traffic center of the world has been driven to Bulgaria. Dr. Edmunds presented some interesting figures regarding the condition of our own country. "The United States," he says, "confiscated three tons in 1931, 17,000 ounces of morphine in one shipment. In 1930, 3000 ounces of heroin alone were seized, while in 1931, 9000 ounces were confiscated, the manufacture and use of heroin being prohibited in this country." He said "there are 120,000 addicts in the United States, 80,000 in Canada, of which number there are 2640 in penitentiaries, 1800 in Leavenworth alone." At the present time the Government has under construction two hospitals for the cure of addiction, one at Lexington, Kentucky, and the other at Fort Worth, Texas.

The second speaker was Dr. Leonard L. Watkins, associate professor of economics. He gave an interesting and illuminating talk on "The Present Banking Situation." Besides speaking encouragingly of the present situation and expressing confidence in President Roosevelt and his plans, he urged the guarantee of deposits to the extent of at least 75 per cent.

The morning session adjourned at noon, at which time a luncheon was served at the Michigan Union. Dean Kraus acting as toastmaster, introduced all present.

The Conference reconvened at 2:00 P.M. with Dr. Russell A. Bunting, professor of oral histology, School of Dentistry. He spoke on the "Present Status of Our Knowledge Concerning the Control of the Decay of the Teeth." He startled the druggists by stating, "there is more harm done with candy bars, than good done with all of the drugs that are sold." Dr. Bunting told of the success obtained in various institutions where periodic examinations and observations are made. Particularly interesting was the important part diet plays in the preservation of the teeth and the control of decay.

The next speaker was Dr. Howard B. Lewis, professor of physiological chemistry, Medical School. He spoke on "Recent Advances in the Study of Hormones and Vitamins." Hormones are supplied in the body by the glands while vitamins are taken into the body. They both act as chemical regulators and are necessary for a healthy body. A concentration of vitamins has been obtained to a degree where $^1/_{1000}$ of a mg. produced the desired effect. This minute dose is termed a gamma. Dr. Lewis stated that the study of this most important subject was still in its infancy and rapid strides were being made in obtaining definite information and facts regarding the use and manufacture of hormones and vitamins.

The last speaker of the Conference was Dr. Nathan Sinai, professor of hygiene and public health. He said pharmacists of to-day have the same problems that have confronted the profession for ages. Back in the 17th century, King James held grocers were just merchants while the pharmacist was a professional man and pharmacy was truly a profession.

Dr. Sinai compared the health of the state (which the last two years ranked the highest in the country) to-day with the past. In 1900 there were 45,000 cases of typhoid, diphtheria and tuperculosis, while in 1931 the total was only 8000, preventative medicine being responsible for this splendid record. The study of medical care and the cost have been taken up by the federal government. Dr. Sinai has made a thorough study of this problem and the medical profession has coöperated generously. He said that it is the task of pharmacy to coöperate with medicine and dentistry. A trip to the College of Pharmacy and other University buildings proved very interesting to many who were eager to seize the opportunity of seeing this institution of higher education that every Michigan resident is justly proud of.

A chicken dinner was served in the Michigan Union after which the assembly adjourned to the auditorium of the Natural Science Building where the regular May meeting of the Detroit Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was called to order by Vice-President Felix Johnson of the University of Michigan.

John Weisel, of Monroe, offered a resolution endorsing Director Parr's plan, which he had presented to President Franklin D. Roosevelt. The resolution was seconded by Dean R. T. Lakey and after Mr. Parr explained his plan it was unanimously adopted and the secretary was instructed to send a copy of the resolution to the President.

Chairman Leonard A. Seltzer, of the nominating committee, reported the following nominees to serve as officers of the Detroit Branch for the ensuing year: *President*, Felix Johnson, U. of M.; *First Vice-President*, Lawrence Maliche, C. C. D.; *Second Vice-President*, Frederick Arnold, D. I. T.; *Student Council*, Hamilton Whitman and Florence Hartsoff, U. of M.; Henry Tyszka and Wm. Hennesy of D. I. T., and Perton Todd and William Blatchley of C. C. D.; *Council of Clerks*, Robert Woonsocket of U. of M., Douglas Robinson of D. I. T., and James Liddell of C. C. D. Secretary Bernard A. Bialk, Treasurer Fred Ingram and *Chairman* of the Program Committee, Dean R. T. Lakey, continue to serve as permanent officers. On motion of Dean E. H. Kraus and Prof. Joseph L. Dorian nominations were closed and the report of the committee was accepted and adopted by a unanimous vote cast by the secretary.

The newly elected president, Felix Johnson, after a few remarks pledging his best efforts to carry on in a manner which will justify the confidence placed in the students in serving as officers of the Detroit Branch—called on Dean Kraus of the College of Pharmacy to introduce the speaker of the evening, Dr. Carl D. LaRue, assistant professor of botany.

Dr. LaRue gave a very interesting talk on his observations on "Drug Collections in the Tropics." He illustrated his talk with many very interesting slides. The speaker had spent three years in Sumatra representing the U. S. Rubber Co., three years in Brazil for the

U. S. Government and three more years in the interest of the Ford Motor Co., devoting most of his time in developing the rubber industry.

Dean Lakey moved a rising vote of thanks to the speaker for his interesting and entertaining presentation, also to Dean Kraus and the faculty of the College of Pharmacy of the U. of M. for their hospitality and the interesting program prepared by them.

Mr. Seltzer offered a motion instructing the secretary to send out a notice of assessment of $1.00 to all members in order that obligations now outstanding may be met. The motion was seconded by Dean Kraus and unanimously adopted. This brought to a close one of the most interesting days in the history of Michigan pharmacy.

BERNARD A. BIALK, *Secretary.*

CONSTITUTION AND BY-LAWS OF LOCAL BRANCHES OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

For Constitution and By-Laws of Student Branches refer to the following issues of the JOURNAL for this year: *Northern New Jersey Branch A. Ph. A.*, March JOURNAL, pages 244–246; *North Pacific Branch, A. Ph. A.*, March JOURNAL, pages 246–248; *California College of Pharmacy Student Branch, A. Ph. A.*, June JOURNAL, pages 572–573.

REPORT OF MEETING OF MARYLAND PHARMACEUTICAL AND BALTIMORE RETAIL DRUGGISTS' ASSOCIATION.

The report herewith of the joint meeting, held August 14th, of the Maryland Pharmaceutical Association and of the Baltimore Retail Druggists' Association includes a report of the National Conference of State Pharmaceutical Associations held in St. Louis, August 8th and 9th. The JOURNAL A. PH. A. is indebted to **Robert L. Swain,** Chairman of the St. Louis Code Committee and editor of the *Maryland Pharmacist* for the following report and thanks are expressed to him for the courtesy.

"The joint meeting of the Maryland Pharmaceutical Association and the Baltimore Retail Druggists' Association, held at the Lord Baltimore Hotel, on Monday night, August 14th, had perhaps the largest attendance in the history of these groups. Nearly six hundred persons were present. The meeting was presided over by President L. V. Johnson, of the State Association, and was called to discuss the Code of Fair Business Practice adopted by the National Conference of State Pharmaceutical Associations at St. Louis on August 8th and 9th.

"The St. Louis code was read by Dr. A. G. DuMez. It was discussed in detail by L. M. Kantner and Robert L. Swain, delegates to the St. Louis Conference. It was pointed out that the Conference was well attended, and that it represented probably 80 per cent of the drug stores of the country. Feeling that such a body was 'truly representative,' as this term is used in the National Industrial Recovery Act, it was said that the code adopted by the St. Louis Conference was most representative of the views of retail pharmacists. The Conference labored two days on the code, and great care was taken to insure that it was in complete accord with the sentiment expressed by those present.

"The following code committee was elected:

A. W. Pauley, St. Louis, Missouri
Denny Brann, Des Moines, Iowa
C. C. Chichester, Macon, Georgia
George W. Mather, Albany, New York
E. F. Kelly, Baltimore, Maryland
Robert L. Swain, Baltimore, Maryland, *Chairman.*

"This committee, it was stated, was to confer with the N. A. R. D. Code Committee, and through joint action, to work out a code really representative of retail pharmacists throughout the country.

"The next speaker was Nicholas Gesoalde, of New York, and he gave a snappy and humorous account of the whole code movement from the very beginning. This talk was illustrated

by witty references to his own experience in pharmaceutical organization work in New York. He seemed to feel that pharmacists might go along with some of the developments of the day, but he advised keeping a weather eye upon the manufacturers and others who had not been notorious in their efforts to help retailers in their troubles. He referred back to the 'courtesy card' movements in New York some few years ago when the retailers of New York sought to work out some coöperative plan whereby profits might be obtained from the sale of advertised lines. Mr. Gesoalde said that he and his committee in charge of the work narrowly escaped imprisonment, so strenuously did certain manufacturers seek to crush the plan. He said that he could not avoid looking at some manufacturers with a fishy eye when they come bearing gifts in place of the club which they had used so many years. His address was rich in experience, and was greeted with prolonged applause.

"Dr. E. L. Newcomb, secretary of the National Wholesale Druggists' Association, New York, and Editor Jerry McQuade, of *Drug Topics*, also of New York, made short but effective talks. Dr. Newcomb stressed the need for coördinated effort throughout the drug industry, and insisted that greater progress, and thus greater benefits, would come from unified action. Mr. McQuade, in his own forceful manner, spoke briefly in behalf of the Drug Institute. He feels that the Institute is the best bet that came before the drug business, in all its branches, in the history of pharmacy. Both Dr. Newcomb and Mr. McQuade were greeted with warm and spontaneous applause.

"Following the asking and answering of questions, the meeting adjourned."

HIGH POINTS OF THE ST. LOUIS CODE.

"Under the St. Louis Code of Fair Business Practice, it is considered unfair business practice:

1. To make any false, misleading, deceptive, untrue, unsubstantiated, unfair or unethical statements in newspaper advertising, or by circulars, letters, window displays or by radio.
2. To misbrand merchandise as to quality or to misrepresent as to price.
3. All schemes, plans, subterfuges, trading stamps, coupons, gifts, prizes, chances, secret discounts, bonuses, rebates, concessions, combination and free deals, and all devices or designs which may weaken or nullify the code.
4. For any retailer to receive or accept from any manufacturer or jobber any secret discount, commission, concession, refund, advertising allowance, unearned discount, or to employ hidden demonstrators.
5. To offer drugs and medicines for sale by others than registered pharmacists.
6. To permit any other than registered pharmacists from owning and operating drug stores.
7. To offer combination or free deals.
8. To substitute one product for another without the purchaser's consent.
9. To permit merchandise to be sold through automatic vending machines and other labor supplanting devices.

"Under the terms of the Code, all retailers will be required to buy at the same wholesale price, and no article can be sold at retail at less than overhead plus five per cent.

"The St. Louis Code is to be coördinate with the N. A. R. D. Code, and in its final form, to be submitted to the NRA for approval. Hearings will be held and changes no doubt made before final acceptance by the President."

HOURS AND WAGES FOR RETAIL DRUGGISTS.

Due to the joint efforts of the National Association of Retail Druggists, the AMERICAN PHARMACEUTICAL ASSOCIATION and the National Conference of State Pharmaceutical Associations the following agreements were concluded with the National Recovery Administration on August 15th. It will cover the hours and wages in Retail Drug Stores until a code of Fair Trade Practice for these stores is heard and approved. The Code will be heard on Thursday, August

24th, at the Department of Commerce Building, Washington, D. C. The following Articles III and IV apply to above.

"(FOR PARAGRAPH 2 OF PRESIDENT'S AGREEMENT. CODE REFERENCE:) ARTICLE III.

For stores open seven (7) days per week, no employee shall be employed more than forty-eight (48) hours per week; provided, however, that no employee shall be employed more than eight (8) hours during any twenty-four (24) hour period; provided, further, that male employees working as waiters shall not be employed in excess of fifty-four (54) hours per week, pending adoption of a permanent code for the restaurant industry; provided, further, that the above maximum hours of labor shall not apply to registered, assistant registered and apprentice pharmacists (meeting the requirements of the state law to become registered pharmacists). The hours of any store in service operation shall not be reduced to below 90 hours in any one week, unless such hours were less than 90 hours per week before July 1, 1933, and in the latter case not to reduce such hours at all."

"(FOR PARAGRAPH 5 OF PRESIDENT'S AGREEMENT. CODE REFERENCE:) ARTICLE IV.

Employees (except messengers engaged in delivering medicinal products and persons under 16 years of age employed as permitted by Section 1, of the President's Reëmployment Agreement) shall be paid not less than $15 per week in the northern part of the United States, nor less than $14 per week in the southern part of the United States, in any city of over 500,000 population, or in the immediate trade area of such city; nor less than $14.50 per week in the northern part of the United States, nor less than $13.50 per week in the southern part of the United States, in any city of between 250,000 and 500,000 population, or in the immediate trade area of such city; nor less than $14 per week in the northern part of the United States, nor less than $13 per week in the southern part of the United States, in any city of between 2500 and 250,000 population, or in the immediate trade area of such city; and in towns of less than 2500 population the wages shall be increased by not less than 20%, provided, however, that the wage need not be in excess of $12 per week; provided, further, that employees with less than 6 months' experience in retail stores shall be paid $2 per week less than the minimum wage provided above. The southern part of the United States is defined as follows: Virginia, West Virginia, North Carolina, South Carolina, Georgia, Florida, Kentucky, Maryland, Oklahoma and Texas. Population for the purpose of this agreement shall be determined by reference to the 1930 Federal census."

Reference is made to the exemptions relative to "maximum hours" requirement in an editorial comment of this issue of the JOURNAL.

CONFERENCE OF PHARMACEUTICAL LAW ENFORCEMENT OFFICIALS.

PROGRAM.

1. Call to Order.
2. Remarks by Chairman, Robert L. Swain.
3. Report of Secretary, M. N. Ford.
4. Report of Finance Committee.

ADDRESSES.

"A Legislative Attempt to Restrict the Opening of New Drug Stores," Hugh P. Beirne, Connecticut.

"The Value of Annual Renewal of Pharmacists' Certificates in the Enforcement of Pharmacy Laws," Walter F. Meads, Iowa.

"A Legislative Attempt to Establish Prescription Tolerances," Robt. P. Fischelis, New Jersey.

"What Privileges Should Be Granted Unregistered Dealers under the Pharmacy Law?" Rowland Jones, South Dakota.

"The Need for Strict Enforcement of the Law," Mac Childs, Kansas.

"Restricting the Practice of Pharmacy to Proper Persons," George W. Mather, New York.

"The Importance of Synonyms in the Enforcement of Drug Standards and Their Relationship to the Enforcement of Pharmacy Laws," Robt. P. Fischelis, New Jersey, *Chairman*, Special Committee.

ROUND TABLE DISCUSSIONS.

"The Proposed Amendments to the National Food and Drugs Act."

"Narcotic Legislation in 1932–1933."

"The Proper Enforcement of Fair Practice Codes for the Drug Industry under the National Industrial Recovery Act, General Enforcement Procedure and Technic."

5. Election and Installation of Officers.
6. Unfinished Business.
7. Adjournment.

EDITORIAL NOTES

Editor: E. G. Eberle, 10 West Chase Street, Baltimore, Md.

Members of the Council, A. PH. A.: S. L. HILTON, *Chairman;* CHARLES H. LAWALL, *Vice-Chairman;* E. F. KELLY, *Secretary;* H. V. ARNY, A. G. DUMEZ, H. A. B. DUNNING, WILLIAM B. DAY, C. E. CASPARI, J. H. BEAL, T. J. BRADLEY, AMBROSE HUNSBERGER. *Ex-Officio Members:* W. BRUCE PHILIP, *President;* ROWLAND JONES, G. H. GROMMET, *Vice-Presidents;* C. W. HOLTON, *Treasurer;* E. G. EBERLE, *Editor of the Journal;* A. G. DUMEZ, *Editor of the Year Book;* J. W. SLOCUM, *Chairman of the House of Delegates.*

Collaborators: The Members of the Council; E. FULLERTON COOK, *Chairman,* U. S. P. Revision Committee; E. N. GATHERCOAL, *Chairman,* N. F. Revision Committee; Chairmen of the Sections, A. PH. A.: W. J. HUSA, W. J. RIVARD, W. PAUL BRIGGS, LEON MONELL, LOUIS GERSHENFELD, CHARLES H. STOCKING, *President,* A. A. C. P.; CHARLES B. JORDAN, *Chairman,* Executive Committee, A. A. C. P.; CLARE F. ALLAN, *President,* N. A. B. P.; HENRY C. CHRISTENSEN, *Secretary,* N. A. B. P. Scientific Section—Board of Review on Papers: *Chairman,* L. W. ROWE, Detroit, Mich.; JOHN C. KRANTZ, JR., Baltimore, Md.; F. J. BACON, Cleveland, Ohio.

THE PROFESSIONAL PHARMACY.

AN ANALYSIS OF PRESCRIPTION DEPARTMENT ACTIVITIES.

BY FRANK A. DELGADO AND ARTHUR A. KIMBALL.

The second installment of this contribution is published in this issue of the JOURNAL; the first part is printed in the July number, pages 671–693.

We are taking the liberty of quoting from "World Trade Notes on Chemicals and Allied Products," Department of Commerce, Bureau of Foreign and Domestic Commerce, August 14, 1933.

"*Prescription Department Activities Analyzed.*—Valuable information that has never before been given will be found in "The Professional Pharmacy," a detailed cost and operations analysis of prescription-department activities of professional pharmacies, made as a major phase of the National Drug Store Survey.

"It is not practical in an announcement this length to outline the contents of the professional pharmacy. However, it might be stated that over 75 per cent of the sales volume of the professional stores studied was actual prescriptions. Sales volume of sample stores averaged $107,000 each. Thirty-five professional pharmacies occupied an average of 1632 square feet. Answers to the following questions are furnished. To what extent, if any, have the specialty type of prescriptions grown over a period of 20 years? Have prescriptions in liquid, capsule and tablet form decreased or increased during the past 20 years? What is the financial outlay necessary to open a new store? What equipment is necessary? What population is necessary to support a professional pharmacy? What is the turnover, gross margin, operating expenses and net profits of professional pharmacies?

"Approximately 1808 pharmacists open new drug stores each year in the United States, and were that part dealing with prescription ingredients brought to the attention of these pharmacists it is believed that a saving of from $100 to $500 per store could be accomplished.

"Two reports by the Bureau of Foreign and Domestic Commerce covering the professional activities of retail pharmacies have come from the National Drug Store Survey. The first dealt with the professional activities of 13 commercial-type drug stores in St. Louis. It was entitled 'Prescription Department Sales Analysis in Selected Drug Stores' and was issued, in 1932, by the U. S. Department of Commerce. Copies can be obtained from the Superintendent of Documents, Washington, D. C., at 5 cents each. The second report, recently completed, is entitled 'The Professional Pharmacy—An Analysis of Prescription Department Activities,' and presents a picture of the pharmacy which specializes in prescriptions and other items related to public health. This report, covering about 80 pages, is being printed in the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, in four installments, July, August, September and October 1933, and will then be available in a paper-bound book . . ."

"The value of the information contained in this report is not believed to be confined to the proprietors of professional pharmacies. It contains much information which should be of practical value to the proprietors of commercial-type drug stores, in increasing their volume

of prescription business and the profit possibilities of their prescription departments. Professors and students in colleges of pharmacy may find herein answers to some of the questions about which there has been conjecture. Drug wholesalers and manufacturers of chemicals, galenicals and pharmaceutical specialties should find the list of leading ingredients, which was compiled after an analysis of 20,000 prescriptions, of particular interest. Pharmacists who are contemplating the operation of a professional pharmacy will find certain information particularly directed to them. It is hoped, therefore, that all branches of the drug profession and trade will be in some way aided by the information presented in this report."

Reprints of "Professional Pharmacy" will be bound in paper cover at 25 cents per copy; 10 per cent discount in quantities of 6 or more and 20 per cent discount in quantities of 100 or more. It is assumed the schools of pharmacy will desire the publication for their students.

ACRIFLAVINE SOLUTION.*

W. A. Woodward reports that the following formula produces a stable preparation:

Acriflavine	1 Gm.
Glycerin	10 ml.
Solution of ammonia	20 ml.
Oleic acid	40 ml.
Chloroform	180 ml.
Liquid paraffin to	1000 ml.

Dissolve the acriflavine in the glycerin with the aid of heat, add the oleic acid and the solution of ammonia, stirring continuously, until the oleate formed has completely liquefied. Allow to stand until the liquid becomes viscous, then transfer it to a dry bottle containing the chloroform, and shake vigorously until dissolved. Pour the chloroformic solution in a thin stream into the liquid paraffin, previously sterilized and cooled to 50° C.

It is possible to use direct heat, provided it is controlled. This hastens considerably the liquefaction of the rather troublesome oleate which, if a steam-bath be used, takes a much longer time to liquefy.

The product is in the form of a clear, mobile reddish liquid. From a theoretical standpoint the principal criticism must be directed against the higher proportion, 18 per cent by volume, of chloroform which the liquid contains. One of the great advantages claimed for acriflavine as a wound dressing is that its antiseptic action is exerted in concentrations too small to affect phagocytosis, and in this solution it should have been anticipated that the chloroform would seriously have interfered. However, the preparation has given complete satisfaction in clinical trials at St. Thomas' Hospital, both in obstetric work and as a wound dressing, and the fact that no pain was experienced tends to show that the presence of the chloroform is not deleterious.

The solution was effective *in vitro* against *B. coli* and, to a less extent, against *Streptococcus hæmolyticus* and *Staphylococcus aureus.*—*Pharm. J.*, April 8, 1933.

* From *The Australasian Journal of Pharmacy*, June 10, 1933.

On account of lengthy reports other matter had to be omitted from this issue of the JOURNAL.

PERSONAL AND NEWS ITEMS.

Hugo Kantrowitz was elected *honorary life member* of the New York Pharmaceutical Association.

Prof. Gustav Bachman, of the University of Minnesota College of Pharmacy, received serious injuries in an automobile accident. While he is making good recovery, he fears that it will prevent his attendance at Madison.

William H. Glover, of the Massachusetts College of Pharmacy, was honored with the degree of Doctor of Pharmacy.

A public square in Cranston, R. I., was named in honor of Clifford E. Tabor, who fell in action in the Argonne Forest. He was a graduate of Rhode Island College of Pharmacy, and cited for bravery by General Pershing. Dedicatory ceremonies were held, the principal speaker being Dean W. Henry Rivard.

J. D. Spurier, of Cleveland, Ohio, has purchased the *Drug Bulletin*, founded in 1879, from E. D. Irvine, well and favorably known member of the AMERICAN PHARMACEUTICAL ASSOCIATION. Mr. Spurier was with Frederick Stearns & Co. for several years; recently he has been associated with *Ure Druggist*. The publication office has been moved to Cleveland.

We are advised of the death, on August 17th, of Mrs. A. L. I. Winne, wife of our fellow-member and Secretary of the Virginia Board of Pharmacy and Virginia Pharmaceutical Association. Sympathy is extended.

OBITUARY.

LEO SUPPAN.

Leo Suppan, professor of Botany and Pharmacognosy in the St. Louis College of Pharmacy, died after a short illness at his home in St. Louis, Mo., July 16, 1933, aged 62 years.

Professor Suppan was born in Jefferson City, Mo., June 7, 1872. He was graduated from the St. Louis College of Pharmacy in 1891, attended the Missouri School of Mines for three years, then the University of New Mexico, where he received the degree, Bachelor of Science. In 1897, he went to Johns Hopkins University for graduate work and, later, studied under Dr. Ernst Schmidt in the University of Marburg, Germany.

In 1903, he became Associate Professor of Chemistry in the St. Louis College of Pharmacy; later, Associate Professor of Pharmacy and, in 1922, Professor of Pharmacognosy and Botany which position he held until the time of his death. In addition to his teaching activities, he was editor of the *National Druggist*. He contributed numerous editorials and papers on scientific and historical phases of pharmacy. Two of his more recent works are worthy of special mention. "Three Centuries of Cinchona" was published in the "Proceedings Tercentenary Celebration of Cinchona," Missouri Botanical Garden, St. Louis, Mo., in 1931. "A Repetitorium of Pharmacognosy," written in conjunction with Noel M. Ferguson, was published in 1932.

He was a member of the St. Louis Art League, The Oriental Society, The Naturalists' Club, The Archæological Society of America, the AMERICAN PHARMACEUTICAL ASSOCIATION, the Missouri Pharmaceutical Association. He was one of the founders of the St. Louis Chemical Society, in 1903, and served as its secretary for several years.

Professor Suppan was conversant in a number of languages. As an inveterate reader, he acquired a most varied and extensive fund of knowledge. He was beloved by students and associates alike, and has left an imprint on many lives. Pharmacy has been much enriched by the life and work of Leo Suppan.

SOCIETIES AND COLLEGES.

WISCONSIN MAPS AND INFORMATION.

Those coming to Madison by auto will be sent a highway map of Wisconsin on which the pictorial history of the state is drawn by Laura Kremers, daughter of Professor Edward Kremers, if they write for same to Ralph W. Clark, Publicity Committee Chairman, 355 Chemistry Building, Madison, Wisconsin. Please write for any information about the convention to the above address.

WOMEN'S ENTERTAINMENT PROGRAM (TENTATIVE), MADISON MEETING.

Golf Arrangements have been made for the guests.

Monday and Tuesday Morning—Reception of visiting ladies.

Tuesday—Luncheon at Madison Club, 1:00 P.M., followed by visit to State Capitol and Historical Museum. (NOTE: Party will leave Hotel Loraine at 12:45 sharp.)

Wednesday—Luncheon and Card Party at Maple Bluff Country Club, 1:00 P.M. (NOTE: Automobiles will leave Hotel Loraine at 12:30 sharp.)

Thursday—Boat Excursion around Lake Mendota, 9:30 A.M. (NOTE: Automobiles will leave Hotel Loraine at 9:00 sharp.)

Friday—Entertainment by Prof. Kehl's Pupils, 10:30 A.M.—Colonial Room, Hotel Loraine.

Friday Afternoon—Shopping Tours. Visits to Madison points of interest. (NOTE: Committee women will be at Hotel Loraine to conduct our guests.)

Saturday—All-day excursion to Devil's Lake and Wisconsin Dells. Three-hour boat trip at Dells in afternoon and Indian Pageant in evening.

OFFICERS OF STATE PHARMACEUTICAL ASSOCIATIONS.

References to other state associations will be supplemented in next issue.

FLORIDA.

Following the meeting of the Florida Pharmaceutical Association, quite a number of pharmacists visited in and around Atlanta. The pharmacists were greeted by Dr. Andre Perez of the Cuban Pharmaceutical Associa-

tion. The entertainments were delightful and much enjoyed by the visitors.

IDAHO.

The Idaho Pharmaceutical Association held its annual meeting at McCall, June 26th to 27th. The following officers were elected: *President*, J. B. Ostrander, Wallace; *First Vice-President*, Clyde Isenburg, Rupert; *Second Vice-President*, Charles Carter, Moscow; *Secrerary-Treasurer*, Elmer B. Williams, Boise. President Thoreson recommended revision of the State pharmacy law; the California Fair Trade bill was endorsed. Lewiston was chosen as the meeting place for 1934.

MAINE.

A feature of the meeting of Maine Pharmaceutical Association was the "Round Table" discussion. The officers for the ensuing year are: *President*, Burton K. Murdock, Kennebunk; *First Vice-President*, Ralph A. Lockhear, Auburn; *Second Vice-President*, Horace T. Poland, Damariscotta; *Third Vice-President*, Ralph C. Trescartin, Phillips; *Secretary*, James H. Allen, Waterville; *Treasurer*, George O. Tuttle, Portland.

MISSISSIPPI.

Following its regular custom the association elevated G. C. Roberts, of Greenwood, from the *First Vice-Presidency* to the *President's office;* raised Lew Wallace, of Laurel, from *Second* to *First Vice-President;* elected J. S. Puller, of Starkville, *Second Vice-President;* and unanimously reëlected Dr. S. B. Key, of Jackson, *Secretary-Treasurer*. The new executive committee is composed of Retiring President McInnis, F. W. Duckworth, Booneville, and Joe A. Moss, Jackson.

As the concluding business of the convention the association voted by a four to one majority to return to Jackson in 1934. The record attendance, splendid program offered and gala round of social functions were asserted factors that brought the enthusiastic support of Jackson's invitation.

MISSOURI.

Quite a number of valuable papers were read at the meeting of the Missouri Pharmacutical Association, and a series of resolutions adopted covering subjects of timely interest. The following officers were elected: *President*, Joe Knight, Lebanon; *First Vice-President*, George C. Egy, Kansas City; *Second Vice-President*, John Emerson Joplin; *Third Vice-President*, John J. Mueller, St. Louis; *Treasurer*, Murray Q. Williams, Warrensburg; *Historian*, Ambrose Mueller, Webster Groves; *Secretary*, W. H. Lamont, 5838 Plymouth Ave., St. Louis; *Honorary President*, E. A. Sennewald, St. Louis.

MONTANA.

Montana Pharmaceutical Association discussed the adoption of a poison register as a move to protect public health. Helena was selected for the 1934 convention city.

The following officers were elected: *President*, H. E. Rakeman, Jr., Ennis; *First Vice-President*, Emil Schoenholzer, Billings; *Second Vice-President*, Donald Wilson, Forsyth; *Third Vice-President*, Howard Craig, Drummond; *Treasurer*, C. A. Challman, Hobson; *Secretary*, J. A. Riedel, Boulder.

OHIO.

The Ohio Pharmaceutical Association held its annual convention on the S. S. Juniata, taking in the World's Fair in Chicago. At the close of the convention, the following officers were elected: *President*, Charles Ehlers, Cincinnati; *First Vice-President*, Thomas J. Ryan, Columbus; *Second Vice-President*, Clark A. Bloom, Youngstown; *Treasurer*, L. W. Funk, Columbus; *Secretary*, Theodore D. Wetterstrom, Columbus.

TENNESSEE.

Tennessee Pharmaceutical Association held its sessions in Chattanooga July 18th and 20th. A new Constitution and By-laws were adopted. An NRA code was discussed and approved. Among the speakers of the Convention were Prof. Paul C. Olsen, and Dr. James L. Bibb of the Hamilton County Medical Society. The provision of the new constitution is that a special one-day meeting of the Association be held in Nashville during the meeting of the state legislature, at which time only legislative problems are to be discussed.

Knoxville was selected for the 1934 meeting and the following officers were elected: *President*, Leslie F. Mitchell, Nashville; *First-Vice-President*, R. R. Ferrell, Memphis; *Second Vice-President*, L. S. Elgin, Knoxville;

Third Vice-President, P. P. Vance, Chattanooga; *Secretary*, William P. Winter, Nashville; *Treasurer*, H. J. Berryhill, Jackson.

(*To be continued*)

TENTATIVE PROGRAM OF JOINT SESSION OF SECTION ON EDUCATION AND LEGISLATION WITH CONFERENCE OF LAW ENFORCEMENT OFFICIALS AND CONFERENCE OF PHARMACEUTICAL ASSOCIATION SECRETARIES.

TOPICS.

"The Pharmacy Board as the Sole Regulatory Body for Pharmacy," R. P. Fischelis.

"A Legislative Attempt to Restrict the Opening of New Drug Stores," H. P. Beirne.

Reports on Enacted and Proposed Legislation Affecting Pharmacy in Various States.

Alabama, S. A. Williams; Connecticut, H. P. Beirne; Colorado, C. J. Clayton; Georgia, R. C. Wilson; Maryland, R. L. Swain; Michigan, C. F. Allen; New Jersey, R. P. Fischelis; Pennsylvania, J. M. Woodside; West Virginia, J. L. Hayman.

TENTATIVE PROGRAM SECTION ON COMMERCIAL INTERESTS.

"The Prescription Defined," Anton Hogstad, Jr.

"Keeping of Records," Walter Scharbach.

"Relation of Professional Pharmacy to the Drug Institute of America," Paul C. Olsen.

"Professional Pharmacy," Robert Gaw.

"Publicity and the Pharmacist," Alice Esther Garvin.

"Profits and Prophets," C. Leonard O'Connell.

"Actual Time and Costs of Some U. S. P. and N. F. Preparations," Henry Brown.

"National Drug Store Survey Speakers from the U. S. Department of Commerce. Drug Retailing," Charles F. Beach.

"Pharmacy," William Rodman.

THE PHARMACY EXHIBIT.

BY H. C. CHRISTENSEN.

The Pharmacy Exhibit is located on the ground floor of the Hall of Science in the Medical group. The easiest method of finding it is to locate the Transparent Man. The Pharmacy Exhibit is on the circular corridor to the left. This is the north end of the building.

The history of the exhibit is briefly: A Local Committee was formed in Chicago, with H. C. Christensen as chairman, to see that Pharmacy was properly represented at the Fair. The space, 1700 sq. ft., with a commercial value of $17,000, was donated by the Fair officials, upon pledge of a proper exhibit. The AMERICAN PHARMACEUTICAL ASSOCIATION was named sponsor and signed the contracts. The Local Committee not only planned and supervised the installation of the exhibit but also raised the necessary funds from all branches of pharmacy. A great share of the credit for fund-raising goes to the very efficient treasurer, J. H. Riemenschneider; Dr. Frank H. Kirby carried out the duties of the secretary most faithfully.

Photographs and descriptions of the exhibit have appeared in the leading journals. See it for yourself. Register at the desk as we want a complete record of all those connected with the drug industry who have visited the Pharmacy Exhibit.

Miss Esther H. Barney, registered pharmacist and superintendent of the Exhibit, will be in charge. Miss Barney is well informed on matters pertaining to the Fair and is a genial hostess.

CANADIAN PHARMACEUTICAL ASSOCIATION.

An interesting program has been arranged for the Canadian Pharmaceutical Association convention to meet at Montreal, August 21st to 24th, and we wish for our Canadian friends a most successful meeting. Our only regret is that their meeting is held so near to the time of that of the AMERICAN PHARMACEUTICAL ASSOCIATION as we are fearful it may interfere with the attendance from Canada. It has always been a pleasure to have representatives present at the annual meeting and we hope to see a number in attendance at Madison. Prof. Charles F. Heebner, of Toronto, is the *Honorary President* of the AMERICAN PHARMACEUTICAL ASSOCIATION.

THE BRITISH PHARMACEUTICAL CONFERENCE.

The 70th annual meeting of the British Pharmaceutical Conference was held in London, July 24th to 27th. The *Pharmaceutical Journal* comments that this year's meeting of the British Pharmaceutical Conference is

noteworthy in many respects. The meetings of the Conference are held every ten years in London and special pains were taken by the Local Committee to mark the importance of the occasion. The Editor has been favored with a program and other illustrated literature of the event. The program is a work of art depicting London and its buildings, showing St. Paul's Church and the River Thames. The cover illustration presents a view of London of 1616 reproduced from a print in the London Museum. The title page has as a design an 18th century pill slab bearing the arms of the Society of Apothecaries and of the city of London.

Succeeding pages show President John Keall and Chairman C. H. Hampshire, of the British Pharmaceutical Society and British Pharmaceutical Conference. Another page contains a welcome to London by the chairman of the London Committee, A. R. Melhuish. A full-page illustration is that of an engraving by J. G. Murray of the painting by W. Hunt, in 1840, of the Laboratory of John Bell & Co., London, reproduced last year in the JOURNAL A. PH. A. Three pages are given over to social functions and one page to the chair presented by the pharmaceutical societies of Australia and New Zealand at the delegates' meeting on Wednesday, July 26th. (See page 661, July JOURNAL.)

A full-page illustration is shown of a drug mill of the Apothecaries Company in 1788, situated in Lambeth Walk, from a painting by Miss M. L. Worley in the possession of the Society of Apothecaries. Four succeeding pages contain illustrations of a mortar inscribed "C. R." and dated 1664, possibly by N. le Febvre, apothecary to Charles II. Drug jar with the arms, crest, mantling and motto of the Apothecaries Company of London, in blue, green, yellow and turquoise. About 1650–1660. Mortar inscribed "Henry Knight, 1618" around the lip and the band around the waist "George Millisente." Cast at Reading. Mortar bearing the date 1663 and the name, "John Battersby, the physician of Samuel Pepys" and the last page shows the old Plough Court Pharmacy, London, built about 1607.

Among the speakers at the banquet were President John Keall, Chairman Dr. C. H. Hampshire and Dr. J. J. Hofman, president of the International Pharmaceutical Federation. Australia, Belgium, Denmark, France, Germany, Holland, New Zealand, Roumania, South Africa, Spain, Switzerland and Sweden were represented by delegates.

PUBLICATIONS RECEIVED.

We are in receipt of the following: A memorial number prepared by the Apothecaries Society of Nürnberg and vicinity, commemorating the period between 1632 and 1932. The booklet is illustrated and aside from dealing with the activities of the apothecaries contains historical references to the city; outstandingly, however, the booklet is concerned with pharmaceutical history.

Reprint contributions to the knowledge of the constituents of *Orthosiphon stamineus* Benth., an inaugural dissertation in preparation for the Ph.D. degree, by CHARLES FEVRIER, apothecary at Neuchatel. The dissertation contains nearly sixty printed pages and the author thanks members of the faculty, Dr. P. Casparis, Dr. H. Zörnig and Dr. Buxtorf.

Pharmaceutical Analyses by DR. C. A. ROJAHN, a contribution from the Institute of Pharmacy and Food Chemistry of the University of Halle, reprinted from the *Pharmazeutische Zeitung*, 1932, volume 77, page 866.

The analyses concern those of secret remedies. The Analyst has drawn on "Gehe's Codex" and other lists of that type for the sources of his research. Eighty-seven classes, each comprising a large number of preparations, are given and speak for the extensive work conducted by Dr. Rojahn.

Biochemical Researches on the Glucides of Chamomile Flowers by DR. CH. BEGUIN, at the University of Zurich, published in a *Pharmaceutica Acta Helvetiæ*, December 12, 1932. The reprint covers thirty pages.

A booklet on the scientific works of Dr. M. Albert Goris, director of the Pharmacy of the Central Hospital of Paris and professor of Galenical Pharmacy of the Faculty of Pharmacy at Paris. The booklet reports the honors which have been bestowed on Dr. Goris and the positions held by him at various periods.

Abstracted references are made of numerous scientific articles and the subjects are quite varied. Thus there are researches in biochemistry, culture of medicinal plants, collective and on individual subjects, studies on fluid extracts, syrups, etc.

Reprint from the *Pharmazeutische Zeitung* on "The Manufacture of Tablets." It is published in book form, the author being ERICH SCHROFF. The publishers are Julius Springer, Berlin, Germany. The price is 90 Rm.

(*To be continued*)